Executive Function at Early School Age in Children Born Very Preterm

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Abstract

Impairments in executive function have been posited to account for some of the poor cognitive and educational outcomes associated with very preterm birth. As part of a prospective, longitudinal study, this research examined executive function in a regionally representative sample of 103 children born very preterm and/or very low birth weight (<33 weeks GA / <1500g) and a comparison sample of 108 full term children at age 6 years (corrected for prematurity). The specific aims of the study were 1) to describe the performance of children born very preterm and full term on a range of executive function measures, 2) to identify the antecedent medical, neurological and socio-familial factors associated with executive function performance within the very preterm group, and 3) to examine linkages between children's executive function performance and their academic achievement at age 6 years.

Children underwent a comprehensive developmental assessment, including standardised tests of IQ and academic achievement in mathematics, reading and receptive language. Additionally, they completed a number of executive function tasks selected to assess verbal working memory (Digit Span), spatial working memory (Corsi Blocks), planning and problem-solving (Tower of Hanoi), selective attention (Visual Search), shifting and inhibitory control (Detour Reaching Box) and sustained attention and inhibition (Kiddie-Conner's Continuous Performance Task; K-CPT). Parents and teachers of these children also completed the Behavioural Rating Inventory of Executive Function and teachers rated children's performance in reading, arithmetic and comprehension in relation to their classroom peers.

Results revealed a pervasive pattern of impairment across multiple measures of executive function in children born very preterm relative to their full term peers.

Specifically, children born very preterm were less likely to be able to complete any backward Digit Span trials ($p<0.05$) and showed lower raw scores on this task ($p<0.1$) than children in the full term group. Children born very preterm showed lower spatial span scores on the Corsi Blocks Task ($p<0.01$). They also showed lower planning performance, as assessed by the Tower of Hanoi ($p<0.05$). Children born very preterm made more inhibitory control/shift errors on the Detour Reaching Box and demonstrated less accuracy in their Visual Search ($p<0.001$) than children born full term. Finally, they showed lower levels of sustained attention on the K-CPT ($p<0.001$). Parents, teachers and examiners rated these children as having greater difficulties across multiple areas of executive function. These differences remained significant after controlling for group differences in socioeconomic status and after exclusion of children with severe cognitive and motor impairments.

Within the very preterm group, antecedent predictors of poorer working memory and planning performance included male gender ($p<0.001$), intrauterine infection ($p<0.05$) and severity of cerebral white matter abnormality on term-equivalent MRI ($p<0.05$). Lower gestational age ($p<0.05$) and male gender ($p<0.001$) were related to poorer executive attention performance. Familial predictors of poorer executive performance included instability in parenting ($p<0.05$), higher levels of parental intrusiveness ($p<0.1$) and lower levels of interactional synchrony ($p<0.05$) between parent and child, recorded at earlier follow-up points. Finally, children's executive function performance was highly correlated with school achievement in reading, arithmetic and language comprehension ($p<0.001$).

Findings suggest a global pattern of executive impairment amongst children born very preterm, with these difficulties placing children at risk for poor academic performance and learning difficulties. Findings also suggest that both neurological pathology and early parenting experiences are important mediators of the relationship between very preterm birth and poor executive function, highlighting the importance of these areas for early intervention.

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List of Abbreviations

ADHD	Attention Deficit Hyperactivity Disorder
BSID	Bayley Scales of Infant Development
CLD	Chronic Lung Disease
CPAP	Continuous Positive Airways Pressure
ELBW	Extremely Low Birth Weight
GA	Gestational Age
IPPV	Intermittent Positive Pressure Ventilation
IUGR	Intrauterine Growth Restriction
IVH	Intraventricular Haemorrhage
K-CPT	Kiddie Continuous Performance Task
MRI	Magnetic Resonance Imaging
NEC	Necrotising Entercolitis
NICU	Neonatal Intensive Care Unit
OR	Odds Ratio
PDA	Patent Ductus Arteriosis
PVL	Periventricular Leukomalacia
RDS	Respiratory Distress Syndrome
ROP	Retinopathy of Prematurity
SES	Socioeconomic Status
SGA	Small for Gestational Age
VLBW	Very Low Birth Weight
WPPSI-R	Wechsler Preschool and Primary Scale of Intelligence-Revised

Chapter 1

Overview of Literature on the Cognitive and Educational Development of Children Born Very Preterm

Technological advancements in the 20th century have led to an increase in survival at both ends of the developmental spectrum. Such advancements present a new medical and psychological challenge of ensuring that a high quality of life accompanies this increase in survival. One area in which this is of importance is in the case of very preterm birth. With advancements in ventilation, thermoregulation and the use of surfactant therapy, the survival rates of these infants increased rapidly during the latter part of the 1900s and greater numbers of children at are now being rescued at younger gestational ages (Briscoe, Gathercole, & Marlow, 1998).

An issue of difficulty in reviewing contemporary literature on the development of children born very preterm is the varied range of criteria used to define this population. Children born <37 weeks gestational age (GA) are generally considered to be born preterm or premature (Ministry of Health, 2004). The term very preterm is generally used to define groups of children born at a GA of <33 weeks. Cut off criteria for the smallest infants are less well defined, with researchers sometimes using 28 weeks and sometimes using 26 weeks as an upper limit criterion for extreme prematurity (Anderson & Doyle, 2003; Marlow, 2004). There is currently a trend for studies to focus on children born very or extremely preterm. Added to this, a raft of studies in the 1980s and 1990s was conducted with groups of children born at low birth weights. These studies tend to include children born <2500g as a criterion for low birth weight (LBW), <1500g as a criterion for very low birth weight (VLBW; Hack et al., 1992; Rickards, Kelly, Doyle, & Callanan, 2001), and <1000g as a criterion for extremely low birth weight (ELBW), although this also varies across studies (Grunau, Whitfield, & Davis, 2002; Taylor, Hack, Klein, & Schatshneider, 1995).

While birthweight has previously been considered a more reliable indicator of immaturity, more accurate ultrasound measures of gestation have resulted in a greater number of researchers using GA as a criterion for preterm birth. As GA and birthweight are generally highly correlated, the consideration of studies pertaining to infants born <1500g and/or <33 weeks GA is likely to present a more complete understanding of the outcomes of these children. For the purposes of this review, specific criteria used to define samples will be provided for the studies discussed. For more general outcomes, these children will collectively be referred to as children born very preterm.

Regardless of how it is defined, the population of children in New Zealand who have experienced very preterm birth has increased. Between 1980 and 1999, the proportion of singleton babies born earlier than 37 weeks GA in New Zealand increased by 37% (Craig, Thompson, & Mitchell, 2002). The greatest relative increase occurred in the rate of children born extremely preterm (<28 weeks GA). Although only 0.5% of births in New Zealand were born under this gestational age bracket in 1999, this reflects an increase of 81.5% over the preceding 10 years (Craig et al., 2002). Children born <32 weeks made up 1% (n = 660) of all live births in New Zealand in 2004, with a similar proportion (n= 561) born VLBW. Of infants born <32 weeks GA, 84% survived the neonatal period. Similarly, 82% of children born VLBW survived to hospital discharge (Ministry of Health, 2004). Similar increases in survival have been reported in other first-world countries. In the USA during the 1960s, fewer than half of infants born between 1000 and 1500g survived. This percentage rose to 90% by the year 2000 (Reichman, 2005). In 2005, 1.14% of live births in the USA were very low birth weight and 1.26% of children were born

<32 weeks gestation (Martin et al., 2007).

There is general agreement that we may have reached the threshold of viability for these infants (El-Metwally, Vohr, & Tucker, 2000; Hack & Fanaroff, 2000). As a consequence, attention is now being directed towards the improvement of longer term outcomes. Very preterm birth and VLBW are clearly established risk factors for a range of severe neurodevelopmental impairments. Ten to 25% of infants born VLBW are reported to have severe cognitive delay (IQ < 2 SDs below normative population mean; Wolke, 1998). In addition, children born very preterm are at high risk of motor and neurosensory impairment. Approximately 40-50% of all cases of cerebral palsy, for example, are associated with very preterm birth (Pellegrino, 1997). Studies have shown that 14-20% of children born very preterm/VLBW experience mild to severe cerebral palsy, including quadriplegia, diplegia or hemiplegia (Hack et al., 1994; Jongmans, Mercuri, de Vries, Dubowitz, & Henderson, 1997; Ross, Lipper, & Auld, 1991), with rates being higher amongst those born extremely preterm or ELBW (Marlow, Wolke, Bracewell, & Samara, 2005; Vohr et al., 2000). Other severe neuropsychological conditions such as seizures, hydrocephalus and microcephaly are also more common amongst children born very preterm (Hack et al., 1994). Although incidences of blindness and deafness are generally below 5%, the risk of children born very preterm/VLBW developing these impairments is 9-15 fold higher than in non-clinical samples (Hack et al., 1994; Marlow et al., 2005).

These more severe difficulties, now well documented, characterise a small subset of children born very preterm who are likely to qualify for intensive intervention. However, a growing corpus of literature recognises that a larger proportion of these children are at increased risk for a broad range of more subtle motor, cognitive and behavioural deficits. These may include attentional, social, motor planning and sequencing, visuo-spatial, and learning difficulties (Foulder-Hughes & Cooke, 2003; Goyen, Lui, & Woods, 1998; Hack et al., 1992; Jongmans et al., 1997; Taylor, Minich, Bangert, Filipek, & Hack, 2004). In terms of their behaviour, children born very preterm are approximately 3 times more likely to meet diagnostic criteria for ADHD than children in the general population (Bhutta, Cleves, Casey, Cradock, & Anand, 2002). In addition, these children often experience social difficulties and peer victimisation (Botting, Powls, Cooke, & Marlow, 1997; Breslau et al., 1996; Horwood, Mogridge, & Darlow, 1998; Nadeau, Tessier, Lefebvre, & Robaey, 2004).

As increasing numbers of children born very preterm enter mainstream schooling, their difficulties are likely to have a significant impact on learning and integration into the classroom environment. Similarly, their difficulties are likely to place increased demands on teachers, educational resources and social services (Ichord, 1993). Thus, a detailed understanding of the specific cognitive and educational challenges facing these children as they transition to school is urgently required. To further illuminate the cognitive challenges of children born very preterm, the following section will discuss research relating to their general cognitive outcomes, as determined by IQ testing. Thereafter, a summary of recent research relating to the learning and educational achievement of children born very preterm is provided.

1.1 Cognitive Outcomes in Children Born Very Preterm

While many children born very preterm/VLBW score in the normal range (within 1 SD of the normed mean) on standardised IQ tests, comparisons with their full term peers show that their average group scores are significantly lower (Anderson & Doyle, 2003; Rose & Feldman, 1996; Winders-Davis, 2003). This is supported by a recent meta-analysis of 15 independent studies conducted with school-aged children between 1988 and 2001 (Bhutta et al., 2002). A total sample of 1556 children born <2500g and 1720 children born at term was included in this analysis. Results of the review showed that all studies favoured the full term control participants and that the mean difference in IQ scores for all studies was 10.85 points. Lower birthweight and gestational age were linearly associated with lower cognitive performance.

Researchers have suggested that these global differences in scores on standardised cognitive tests may come about because a subsample of children born very preterm are at elevated risk of severe cognitive impairments (Bohm, Kats-Salamon, Smedler, Lagercrants, & Forssberg, 2002). Several studies of different age groups indicate that the likelihood of a child born <1500g having severe cognitive difficulties, defined as a score <2 SDs below a normed or control group mean, is higher than that of a child born at term (Horwood et al., 1998; Rickards et al., 2001; Ross et al., 1991; Short et al., 2003; Taylor et al., 2004; van Baar, van Wassenaer, Briet, Dekker, & Kok, 2005; Weindrich, Jennen-Steinmetz, Laucht, & Schmidt, 2003). Rates of severe cognitive impairments in these studies vary from 7-16%. For example, Ross et al. (1991) found that 8% of a group of children born VLBW (<1500g) scored below 70 on the *Wechsler Intelligence Scale for Children* (WISC-R Wechsler, 1974) when assessed at age 7-8 years, as opposed to only 1% of the term-born control group. In contrast, Short et al. (2003) reported a proportion of 16% of children born VLBW with severe cognitive impairment at age 8 years, relative to 3% of children born at term. The later study employed the *WISC-III* (Wechsler, 1991). Differences in rates of impairments across studies may come about as a result of different samples studied or the use of newer test norms. Nonetheless, studies generally report a much higher rate of severe cognitive impairment in children born very preterm than the rate of approximately 2.3% in the general population (Wolke, 1998).

Other studies indicate that the likelihood of milder impairment, generally defined as an IQ score greater than 1.0 SD below the normed mean or mean of a full-term comparison group, is also high (Rickards et al., 2001; Ross et al., 1991; van Baar et al., 2005; Weindrich et al., 2003). For example, the Bavarian Longitudinal Study compared the cognitive performance of children born <32 weeks GA (n = 264), a group of matched control children (n = 264) and a regionally representative comparison group (n = 311) at age 6 years (Wolke & Meyer, 1999). Findings showed that children born very preterm were between 2 and 2.5 times more likely to have mild intellectual impairment, based on their performance on the mental processing subtest of the *Kaufmann Assessment Battery* (Kaufman & Kaufman, 1983).

Discrepancies in cognitive performance of groups of children born very preterm may persist even when children with mild or severe impairments are excluded from analyses. In one study, 85 children born between 500 and 1000g were compared with 124 term-born control children at 12 yrs (Saigal, Hoult, Streiner, Stoskopf, & Rosenbaum, 2000). Despite the fact that children with cognitive impairment (IQ below 85) were excluded from analysis, mean group differences in IQ scores remained significant, with the children born preterm scoring an average of 5 points below term born controls. This suggests that differences in global cognitive scores probably arise due to a downward trend in the scores of those born preterm rather than due to the effect of a few outliers who obtain particularly low scores and thereby pull the overall mean down.

In summary, research has established that there is a downward shift in IQ scores in groups of children born very preterm, with differences in overall scores being between half a standard deviation and one standard deviation in magnitude, depending on the nature of the sample (Bhutta et al., 2002). It also appears that children show increased risk for both severe and more mild impairments in cognitive functioning.

1.2 Academic Achievement Outcomes in Children Born Very Preterm

Along with impairments in cognitive development, longitudinal and cross-sectional studies have demonstrated higher rates of academic under achievement and learning disability in groups of children born very preterm. Generally, these studies have operationalised academic achievement in three different ways. The first method entails the comparison of mean performance scores of children born very preterm relative to normative mean scores or full term control group performance scores (Breslau, Johnson, & Lucia, 2001; Breslau, Paneth, & Lucia, 2004; Klein, Hack, & Breslau, 1989; Ross et al., 1991; Saigal et al., 2000; Wolke & Meyer, 1999). A second group of studies have examined rates of learning disabilities amongst samples of children born preterm (Cherkes-Julkowski, 1998; Grunau et al., 2002; Litt, Taylor, Klein, & Hack, 2005; Saigal et al., 2003). These studies employ both achievement-based definitions and discrepancy-based definitions of learning disability. Those that use an achievement-based criterion define learning disability as the attainment of a low score on standardised achievement tests, regardless of IQ. In contrast, those that use a discrepancy-based definition define learning disability as a marked discrepancy between IQ and achievement. A third method by which achievement is examined is by way of teacher, parent and participant report of children's school progress, use of special education services or level of education (Cooke, 2004; Hack et al., 2002; Horwood et al., 1998; Tideman, 2000).

Research studies utilising the first method have reported discrepancies in the mean performance of children born very preterm and full term on standardised tests such as the *Woodcock-Johnson Tests of Achievement* (Woodcock & Mather, 1989), the *Wechsler Individual Achievement Tests* and other standardised measures (Hack et al., 1992; Klebanov, Brooks-Gunn, & McCormick, 1994b; Klein et al., 1989; Ross et al., 1991; Wolke & Meyer, 1999). Generally, these studies examine the key curricular domains of reading and mathematics achievement, although some have also examined vocabulary or specific pre-requisite learning skills related to phonological processing and language comprehension. For example, Wolke and Meyer (1999) examined children's understanding of grammar and syntax using a German language test in the Bavarian cohort described above. They also examined sound production, phoneme identification and letter-number naming in this group of 6 year olds. They found that the mean language scores of children in the very preterm group were lower than their peers and that children born very preterm were approximately 3 times more likely to perform in the lowest 10th percentile for all tasks administered. Given these difficulties in pre-requisite skills related to school tasks, it is not surprising that lower scores have also been reported for broad tests of reading, mathematics and spelling (Hack et al., 1992; Kilbride, Thorstad, & Daily, 2004; Klein et al., 1989; Ross et al., 1991; Taylor, Klein, Drotar, Schluchter, & Hack, 2006).

Apart from these global academic difficulties, there is some suggestion that children born very preterm are particularly prone to difficulties in mathematics, with most studies showing higher effect sizes for the relationship between very preterm birth and mathematics achievement (Breslau et al., 2001; Hack et al., 1992; Klein et al., 1989; McGrath & Sullivan, 2002; Short et al., 2003; Taylor et al., 1995). This was argued by Klein et al. (1989), based on the study of a cohort of 65 children born VLBW (<1500g) and 65 children born full term who were matched for gender, age and ethnicity at 9 years of age. These authors employed the *Woodcock-Johnson Tests of Achievement* (Woodcock & Johnson, 1977) to examine reading and mathematics achievement. They found that children in the very preterm group obtained lower mean scores for all subtests. However, while group differences in reading were not significant when they excluded children with IQ scores <85 from their analyses, the differences in mathematics remained significant. Statistically controlling for IQ also did not completely account for group differences in mathematics achievement. It appears, therefore, that mathematics may be an area where children born very preterm are more likely to have difficulty, even when general cognitive ability is in the average range.

Research studies using the second method of examining academic achievement have generally shown higher rates of learning disability amongst children born very preterm (Cherkes-Julkowski, 1998; Grunau et al., 2002; Johnson & Breslau, 2000; Litt et al., 2005; Ross et al., 1991; Taylor et al., 1995). As an illustration, Litt et al. (2005) employed both an achievement-based (scores lower than 90) and a discrepancy-based (scores more than 1 SD below the expected score of the child, based on their IQ) definition of learning disability when assessing a sample of 31 children born <750g (ELBW), 49 weighing 750-1500g (VLBW) and 52 full term classmates. Children were assessed with the *Woodcock-Johnson-R* (Woodcock & Mather, 1989) reading and arithmetic composite subtests at age 11 years. Children with IQ scores <80, neurosensory impairments or identified neurodevelopmental impairments were excluded from this study. Using the achievement based definition, 15% of children in the ELBW group, 12% of children in the VLBW and 4% of children in the full term group met the criterion for a learning disability in reading. The rates for mathematics and combined reading and mathematics disabilities were 14%, 5% and 3% and 25%, 10% and 7% respectively. However, using a discrepancy-based definition, the only difference was between the rate of learning disability in mathematics in the ELBW (40%) relative to the full term group (20%). Again, these findings suggest higher rates of impairment in children born very preterm, with specific difficulties independent of general cognitive function in mathematics.

Higher risks of learning difficulties have been replicated across international samples. One study examined learning outcomes in children born 500-1000g. Samples from New Jersey, Central Ontario, Bavaria and Holland were compared. The survival rates for children born this small were similar across the cohorts (45-49%), although there were differences in the degree of perinatal intervention given to these infants. Across these cohorts, high numbers of children (38-56%) achieved IQ scores >1 SD below the standardised mean during assessments administered between the ages of 8 and 11 years. Using a similar criterion on achievement tests, high rates of children were shown to have impairments in reading (19-54%), mathematics (24-69%), and spelling (15-40%). Between 39 and 62% of these children were receiving special educational interventions. Unfortunately, the lack of control data in this study makes it difficult to determine the relative risk of impairment in this group. Given that the former studies report rates of learning disabilities of less than 10% in full term samples (Ross et al., 1991), these rates appear particularly high. These and other studies (Cherkes-Julkowski, 1998; Grunau et al., 2002) suggest that the prevalence of learning disabilities amongst children born very preterm is higher than in the general population even in the absence of severe cognitive or neurological impairment.

Along with the employment of these standardised IQ and achievement tests, the third method that researchers have used to assess educational achievement is through the administration of self and observer report instruments to parents, teachers and study participants, questioning them about levels of education attainment, repetition of grade levels and use of special educational services. Studies using these measures have reported high rates of attendance of special schools and extra educational services, as well as higher levels of grade repetition and failure in groups of children born very preterm (Dahl et al., 2006; Rickards et al., 2001; Ross et al., 1991; Saigal et al., 2000; Saigal et al., 2003; Schneider, Wolke, Schlagmuller, & Meyer, 2004; van Baar et al., 2005). This is exemplified in a nationally-based sample of children born <1500g in New Zealand in 1986. The data from the sample of 298 very preterm participants was compared with data from the 8-year follow up of the Christchurch Health and Development Study. Teachers reported that children born preterm were receiving more educational assistance (24.8% vs. 9.4%), and were more likely to be in a special school, class or unit (6.2% vs. 1.1%). Children in the preterm group were also significantly more likely to be rated by teachers as performing below average in reading, mathematics, spelling, writing and physical education.

Across the above studies of academic achievement, there is increasing evidence for a dose-response effect of the extent of prematurity. Indeed, one study demonstrated linear relationships between decreasing birthweight, decreased reading and mathematics achievement scores and increased grade repetition and educational service use (Klebanov et al., 1994b). Similarly, differences in effect sizes are evident when examining studies by Klein et al. (1989) and Breslau et al. (2001), who assessed children born LBW (<2500g), to studies by Grunau et al. (2002) and Saigal et al. (2000), who assessed children born ELBW (<1000g). The effect sizes for the group discrepancies in achievement test performance in the former studies range from 0.2-0.88, while those for the later studies show effect sizes above 1. These findings indicate that children born least mature and most medically compromised are at greater risk for more varied and severe academic difficulties at later ages.

Although few studies have continued follow-up of children born very preterm into early adulthood, some of these studies provide further evidence for a long term impact of very preterm birth on educational outcomes. Using self-report measures of educational attainment, two studies of young adults born very preterm reported that significantly fewer had graduated from high school than full-term comparison participants (Cooke, 2004; Hack et al., 2002). Additionally, these studies indicated that fewer adults born preterm had completed tertiary education. It must be acknowledged that other studies have not demonstrated discrepancies in educational attainment by early adulthood (Saigal et al., 2006; Tideman, 2000). One difficulty in comparing these studies in relation to the cohorts of children born more recently is that these adults were born at a time when fewer infants survived, making it possible that those children who did were the stronger or more resilient infants. Given recent advancements in medical technology, it is likely that those children who survive today are often less healthy and that these studies cannot be generalised to more recent cohorts.

A compelling finding from the Bavarian Longitudinal study was afforded by the inclusion of an academic self-concept measure at ages 6 and 8 years (Schneider et al., 2004). Children who were born full term and VLBW showed improvements in their academic self-concept over time. However, children born ELBW (<1000g) showed decreased academic self-concept at age 8 years. Such findings are evidence for an impact of academic challenges on the long-term sense of wellbeing of children born very preterm, suggesting that they may reduce children's self-esteem. Hence, developing an improved understanding of the early cognitive skills that may jeopardise learning in this group of vulnerable children is likely also to have long-term consequences for quality of life.

1.3 Methodological issues

While cumulative study findings indicate that children born very preterm are more likely to experience cognitive and academic difficulties, conclusions and suggestions for intervention are limited due to several methodological and design issues. These issues are broadly related to sampling and retention, lack of longitudinal follow-up, confounding factors and measurement. Such problems make it difficult to make direct comparisons across studies and limit the generalisability of study findings. Issues are considered in more detail below.

1.3.1 Limitations in Sampling and Retention

As discussed, one of the major issues that makes studies of children born preterm difficult to compare is the failure to use consistent criteria to define the population. This makes it difficult to make direct comparisons across studies. While authors generally report their inclusion criteria with regard to gestational age and birthweight, fewer report the numbers of children born appropriate for gestational age. This is an important limitation because children who are born very preterm sometimes suffer intrauterine growth restriction (IUGR), which can make them small for their gestational age (SGA). This means that they are more than 2 SDs below the average birthweight for their expected gestational age. Children born SGA may be at a greater risk of poor outcome than those born at the appropriate birth weight for their gestational age (Lagercrantz, 1997). One study of reported that 29% of their sample had experienced IUGR (Klein et al., 1989). However, this factor was not considered in the analysis of academic achievement outcomes. It is possible that high rates of growth restriction in this sample may have influenced study findings.

In addition, many studies do not adequately document recruitment rates or characteristics of families who failed to be recruited when reporting the characteristics of their samples. This can pose a difficulty in terms of the representativeness of the samples studied. A poor rate of sample recruitment may result in sample selection bias. Similarly, not all studies adequately report the rates of attrition in their studies or the reasons for sample attrition over time (Aylward, 2002; Siegel, 1994; Wolke, 1998). Research has shown that participants who fail to be recruited at follow up are often those with lower initial scores on standardised tests and those in the lowest brackets of socio-economic status (de Graaf, Bijl, Smit, Ravelli, & Vollebergh, 2000). Therefore, attrition may result in the under retention of families with fewer educational and financial resources. Levels of participation in the academic achievement studies reviewed ranged from less than 50% to above 90%. These differences in sample recruitment and retention are likely to influence patterns of findings across studies.

The effects of recruitment and retention issues are highlighted in the findings of two recent studies describing the outcomes of prematurity at young adulthood (Hack et al., 2002; Saigal et al., 2006). The first study reported that 74% of a sample of young adults born <1500g had graduated from high school (Hack et al., 2002). However, the second study reported that 82% of a sample of young adults born <1000g had graduated from high school (Saigal et al., 2006). Findings from these studies therefore produce a conflicting representation of the long-term consequences of VLBW. Careful inspection of the respective samples reveals that, not only do the inclusion criteria for the studies differ, but that more participants in the second study were from socioeconomically disadvantaged households. In addition, only 57% of participants initially involved in the first study were re-recruited at follow up, whereas the second retained 90% of their sample to adulthood. These issues highlight the importance of accounting for socioeconomic differences across samples, as well as the importance of careful inspection of recruitment and retention rates when interpreting study findings.

Another key methodological limitation of former studies is a failure to recruit appropriate control groups. Many researchers have relied on test norms to assess the abilities of groups of children born very preterm. This may lead to an overestimation of the abilities of these children, especially if norms are out of date. The phenomenon known as the Flynn effect, a gradual rise in IQ in the general population over time, means that norms become outdated quickly (Kanaya & Ceci, 2007). One study showed that a full term control group, matched for socioeconomic status (SES) to a group of children born between 24 and 31 weeks GA, obtained mean performance scores ranging from 111-114 on the *Bayley Scales of Infant Development* (Bayley, 1969) between 6 and 24 months of age (Gross, Slagle, D'Eugenio, & Mettelman, 1992). The standardised mean for this scale is 100. Thus, when the test norms were used, 70% of children in the very preterm group were classified as functioning in the average developmental range at 24 months and 10% were classified as seriously delayed. However, when compared to the mean of the control group, <50% of children in the very preterm group were classified as functioning in the normal range and 20% were classified as delayed. These findings highlight the importance of a control group for the adequate interpretation of scores.

A final issue with regard to sampling is that many studies that assess children born very preterm on a longitudinal basis do not recruit control groups at early ages. Instead, they generally obtain groups of control children from the general community or from the schools or classes of those born very preterm at the time of follow up (Marlow, Hennessy, Bracewell, Wolke, & Group, 2007; Taylor et al., 2006). Follow-up of control children in parallel to those born preterm is an advantage in that it allows for the study of changes in development over time and for greater description and identification of common and divergent social and familial influences, which may also vary across time.

1.3.2 Lack of Longitudinal Follow-up

Related to this, a second major research design issue concerns the need for long-term follow up studies of populations of children born very preterm. While children in a preschool environment often rely on parents and teachers for external self-regulation, the classroom environment necessitates long periods of sustained attention, the application of new strategies and sophisticated information processing. Thus, it is possible that sleeper effects may emerge, whereby children who may not have demonstrated cognitive weaknesses at younger ages may have difficulties overcoming these new developmental challenges. Indeed, there is some suggestion that cognitive difficulties may become more pronounced as children born very preterm mature. One study showed that the mean score of a group of children born very preterm (<33 weeks GA) on the WISC-R (Wechsler, 1974) was 104 at age 8 years (O'Brein, Roth, Rifkin, & Wyatt, 2004). By age 12-14 years, the mean performance in the same group of children had dropped to 95. Similarly, 85% of children achieved scores >85 at age 8 years, while this percentage dropped to 68% at age 12-14 years. Interestingly, there was no change in the percentage of children who obtained scores <70, suggesting that the majority of movement was from average to mildly impaired performance. Such findings highlight the importance of a longitudinal study up to and beyond transition to school when considering the outcomes of children born very preterm.

1.3.3 The Role of Confounding and Explanatory Factors in the Development of Children Born Very Preterm

A third methodological and design issue concerns the role of individual factors that may confound, mediate or moderate the associations between prematurity/VLBW and low achievement outcomes. Perhaps the most important issue is that very preterm birth is often associated with lower SES (Martius, Steck, Oehler, & Wulf, 1998). Additionally, low SES is a well-established correlate for poor cognitive and educational performance (Johnson, McGue, & Iacona, 2007; Walker, Petrill, & Plomin, 2005). Thus, while research has shown an association between premature birth status and poor outcomes in groups of children born preterm, it is less clear whether the lower mean scores reflect an over-representation of children born very preterm in families who are challenged by the stressors associated with lower SES.

In some studies, researchers have been careful to match children of different SES across very preterm and full term control groups (Bayless & Stevenson, 2006; Herrgard, Luoma, Tuppurainen, Karjalinen, & Martikainen, 1993; Katz et al., 1996; Ross, Lipper, & Auld, 1996; Vicari, Caravale, Carlesimo, Casadei, & Allemand, 2004). However, this introduces a difficulty with respect to the representativeness of samples, in that the full term groups of low SES may no longer be representative of the general population. In addition, between-group matching constricts the exploration of interactive or moderating effects of SES on the outcomes of very preterm birth, in that variance is 'controlled' away (Steinberg, Darling, & Fletcher, 1995). Nonetheless, the role of group differences in socioeconomic circumstances in relation to low IQ and poor learning outcomes is an important factor to consider.

Other variables that may affect findings include correlates of very preterm birth such as cerebral palsy and visual-motor integration difficulties (Bracewell & Marlow, 2002; Feder et al., 2005; Foulder-Hughes & Cooke, 2003; Jongmans et al., 1997). Ophthalmological problems, including myopia, strabismus and refractive disorders, are also common (Repka, 2002). While such comorbid factors are often difficult to tease apart from intellectual processes, their influence on achievement outcomes warrants further consideration. Specifically, there is a need for researchers to examine whether group differences in achievement may arise due to the influence of a small group of very preterm children with moderate to severe impairment across multiple domains (Pasman, Rotteveel, & Maassen, 1998). In addition, present research should aim to explore the influence of specific risk factors associated with prematurity in order to identify children who may be most at risk and most in need of intervention. Potential confounds and correlates of very preterm birth in relation to specific cognitive outcomes will be afforded further consideration in Chapter 4.

1.3.4 Issues Related to Measurement

A fourth area of concern involves the measurement of cognitive and educational outcomes of children born very preterm. One important issue is whether to use adjustment to age for prematurity when testing. Many tests allow for an adjustment of scores according to the extent of prematurity, applying the concept that children born very preterm are biologically less mature than their term-born peers. In these studies, researchers may use standardised test age norms that are based on an estimated full term birth date, as opposed to norms based on the actual birth date of the child. Often, researchers will employ a mixed method, adjusting for prematurity until age 2 years and ceasing to do so thereafter (Wilson & Cradock, 2004). However, this assumes that children born very preterm will have ‘caught up’ developmentally with their peers by this age, an idea that has not been supported by studies that show that discrepancies in performance may become more pronounced with age (O'Brein et al., 2004). Whilst adjustment for prematurity is an issue of contention, it does allow children born very preterm an advantage, with some authors arguing that the use of chronological age can misattribute immaturity to developmental delay and result in an overestimation of difficulties in children born very preterm (Wilson & Cradock, 2004). The documentation of development after adjustment for prematurity provides a more conservative estimate of the effects of preterm birth in that allowance is made for immaturity.

A further issue with regard to measurement is that it may lack ecological validity. Studies typically rely only on testing in a laboratory situation in order to determine developmental outcome. This is an issue because children's performance on tests in a laboratory situation is likely to be influenced by the artificial nature of the situation. This can be problematic in several ways. Conceivably, children's performance on these tests is scaffolded by the structured, individually-based nature of the interaction with the examiner. Thus, it may not adequately reflect children's performance in a busy, classroom environment, where less guidance is available. Standardised tests and measures are also often normed on international samples, which presents challenges with regard to the ecological validity of these measures in a New Zealand setting.

Similarly, researchers often rely on a single source in order to measure children's cognitive or behavioural functioning. Reliance on parent report measures is unlikely to yield a clear representation of children's ability in that parents may have different expectations or different attitudes towards children, which are likely to bias their responses. Indeed, some evidence exists to show that parent report and laboratory assessment findings are not consistent in children born very preterm (Winders-Davis, Burns, Snyder, & Robinson, 2007). This being the case, it is preferable that input from several independent sources be used to assess children's development in order to attain a reliable, externally valid understanding of their development across contexts.

Finally, studies of children born very preterm have predominantly made use of standardised measures, such as the *Bayley Scales of Infant Development* (BSID;

Bayley, 1993) and the *Wechsler Intelligence Scales for Children* (WISC; Wechsler, 1974) to assess children born preterm. More recently, researchers have recognised that the utilisation of these tests and the reporting of mean scores does not always accurately describe the specific cognitive difficulties experienced by children born very preterm (Aylward, 2002). Results of such tests provide limited information about the specific cognitive challenges that may make learning difficult for these children. Standardised tests are made up of a composite of subtests and represent an average of these skills. A child who is weak in one area and strong in others may obtain an average score. Furthermore, the results of these measures do not accurately describe the types of skills that children are engaging when approaching such problems. There have therefore been increased calls for a shift in measurement in the follow-up of groups of children born very preterm/VLBW. While standardised tests continue to be incorporated in follow up research, reports of the global assessments of IQ are gradually being accompanied by precise measurement of specific neuropsychological skills.

Research has consistently demonstrated that children born very preterm/VLBW are at increased likelihood of having both severe and more subtle neurodevelopmental impairments. These children show significantly lower mean performance across standardised cognitive measures, as well as a greater likelihood of scoring in a range suggestive of mild or severe cognitive impairment. Of particular importance for public health, education and families, these difficulties are apparent in children's academic performance, with higher numbers of these children experiencing learning difficulties in reading, mathematics and spelling, when compared to their full term peers. There is also some suggestion that achievement difficulties may be particularly apparent in mathematics, even for children who show comparable general cognitive performance in relation to their full term peers.

However, this review of studies has also highlighted several methodological and measurement issues that need to be addressed in future studies. In lieu of these issues, the current study made use of prospective, longitudinal data from a regional cohort of children born very preterm. The study is rigorous in the documentation of the early medical and neurological characteristics of the sample. In addition, a sample of full term control participants were also recruited at an early age in order to meaningfully compare the performance of these children with their age-matched peers living in the same community. Recruitment and retention rates for the sample have been and continue to be high. Furthermore, the study employs both standardised and more novel neurodevelopmental measures in order to more fully assess specific areas of cognitive difficulty that children born very preterm may experience. Further consideration of the specific areas of cognition assessed and the reasons for an assessment of these areas of neurodevelopmental function is provided in subsequent chapters.

Chapter 2

Executive Function

In cultures worldwide, the period between 5 and 7 years of age is seen as a time when children can be assigned greater responsibility and take on new roles. Psychologists have deemed this period ‘the 5 to 7 year shift’ (Sameroff & Haith, 1996) and recognize it as a time when children are able to sustain attention for greater periods of time, process more complex information and start to use metacognitive skills to regulate their own learning (Samango-Sprouse, 1999). Indeed, the transition to formal schooling places substantially increased expectations on children to exercise these strategies. In developmental psychology, researchers have become increasingly interested in the cognitive mechanisms that regulate problem solving and goal-directed behaviour. These skills are known as executive functions.

Executive functions have been defined as the set of processes that allow us to engage effectively in flexible and conscious goal-directed behaviour (Anderson, Levin, & Jacobs, 2002; Hughes, Graham, & Grayson, 2004; Lezak, 1983; Mellier & Fessard, 1998; Welsh & Pennington, 1988). These processes may include the ability to plan and initiate activity, hold a sequenced problem-solving set in mind while resisting interference, flexibly adapt our behaviour and evaluate outcome (Denckla, 1996; van der Sluis, de Jong, & van der Leij, 2007). Executive function is an organising theoretical construct to describe the utilisation and coordination of these various cognitive activities to assist in the achievement of complex or novel tasks (Elliot, 2003; Klenberg, Korkmann, & Pekka, 2001).

The concept of executive function emerged from neuropsychological and cognitive literature. In early observations of both adults and children with damage to the prefrontal cortex, Luria (Luria, 1973; Luria & Tzvetkova, 1978) stressed difficulties in the organisation of behavioural and cognitive responses. He noted that behaviours were often stereotypical or perseverative and that they appeared to be governed by environmental stimuli rather than by an internal system. Luria commented that patients with damage to the prefrontal areas seemed unable to switch effectively from one memory trace to another, making it difficult for them to show fluency in their behaviours (Luria, 1965, 1973).

Luria also stressed that impairments in those with injury to the frontal lobes were most evident on complex problem-solving tasks, which required the individual to segment the problem into a series of sub-problems or to analyse the information carefully prior to answering a question. He found that patients with damage to the prefrontal cortex tended to make guesses or to give an answer based on a stimulus that triggered their attention rather than employing intellectual deduction to reach a solution. Thus, they did not seem to check their results against a goal (Luria, 1973). Therefore, Luria's work established the importance of the frontal cortical regions for the regulation of both behavioural and mental activity. His writings highlight the importance of the frontal lobes in maintaining focus on the relevant aspects of our environment and in working fluently towards a goal. Implicit in these descriptions is the idea that the frontal lobes are not involved in automatic processes that are elicited by stimuli in the environment. Instead, processes that involve a planned, goal-directed response to a novel stimulus or problem in a flexible manner are emphasised (Dennis, 1991; Mellier & Fessard, 1998).

Other researchers have also stressed the importance of the anterior regions of the brain for the regulation of complex mental activity. Studies of children and adults with lesions to the frontal areas have shown that there is a breakdown in the ability to regulate and self-monitor, with behaviour appearing to be environmentally determined, rather than internally regulated (Eslinger, Flaherty-Craig, & Benton, 2004; Grattan & Eslinger, 1992). As a group, adults with lesions to the frontal regions often have difficulty in thinking flexibly or in an abstract manner, have difficulty in regulating attention and sequencing activity in a goal-directed manner and are poor at initiating activity (Banich, 2004). These deficits become apparent when they are asked to perform complex neuropsychological tasks that involve planning and goal-directed forethought (Jonides & Smith, 1997; Miyake et al., 2000).

Executive processes have also interested cognitive theorists, who view underlying processes as being guided by a central executive or a supervisory attention system. This system regulates cognitive activity during situations that are novel or complex (Shallice, 1988, 2002). In general, cognitive theorists believe that we are able to employ learned schemas during habitual activities. However, when there is competition between schemas or when complex situations require several schema need to be integrated, an hierarchically superior supervisory or executive system needs to exert conscious, top-down control.

Thus, both neuropsychology and cognitive psychology have stressed the importance of an hierarchically organized system of executive control in the brain, which assists in the regulation of complex, goal directed mental activity. This system allows for flexibility in thinking, sequencing of complex information and the inhibition of activities or stimuli that are not conducive to the successful completion of goal-directed tasks.

2.1 Components of Executive Function

Executive function has been conceptualized in many different ways, with several people presenting different views as to how it may operate. An homogenous definition of executive function has recently been criticised, with researchers arguing that one construct does not sufficiently describe the complexity of impairments seen in children and adults with difficulties in executive function (Baddeley, 2002; Kimberg, D'Esposito, & Farah, 1997). Some researchers view executive function as a functional construct, which draws on various processes involved in problem-solving, including the anticipation or formation of a goal, planning to reach that goal, carrying out the behaviours and the subsequent evaluation of performance (Lezak, 1983; Zelazo & Muller, 2002). While these problem-solving frameworks are useful in terms of helping to break down the different stages of analysis for which children may invoke executive strategies, they do not delineate the cognitive mechanisms by which effective executive function is achieved. Thus, although executive function may represent a theoretically useful, overarching latent construct, it is probably accomplished with the aid of a number of component skills (Kimberg et al., 1997).

This componential view of executive function is supported by research that shows that different developmental disorders are associated with deficits in different types of executive function. For example, children with ADHD usually demonstrate deficits on tasks purported to tap inhibitory control, while their performance on tasks that assess fluency or mental flexibility is usually similar to that of their peers. Children with autism, however, are more likely to struggle with tasks that require set-shifting and their deficits are generally more pronounced, suggesting different profiles of executive impairment in each of these two developmental disorders (Geurts, Verte, Oosterlaan, Roeyers, & Sargeant, 2004; Ozonoff & Jensen, 1999; Pennington & Ozonhofff, 1996).

Support for a multi-component view of executive function also comes from factor analytic studies. In these studies, researchers have administered batteries of tests to children of various ages (3-21 years) and then performed principal components analysis (PCA) or confirmatory factor analysis (CFA) on the executive function variables to determine whether they represent a common underlying construct as opposed to multiple factors. In general, these studies have tended to support the later argument, but have also acknowledged an underlying unity or common latent construct for executive function tasks, with correlations between tasks being small to moderate. Studies using PCA have variously supported separate dimensions of inhibitory control (Brocki & Bohlin, 1999; Levin et al., 1991; Welsh, Pennington, & Groisser, 1991), planning (Levin et al., 1991; Welsh et al., 1991), fluency and processing speed (Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001; Brocki & Bohlin, 1999; Welsh et al., 1991) and working memory (Brocki & Bohlin, 1999).

However, it must be acknowledged that these studies rely on the researchers' interpretations of what observed constructs may represent and tasks have varied considerably across studies. More recently, researchers have employed CFA to try to confirm their assessments of the latent constructs that executive tasks may be tapping. These studies have shown support for a separate executive dimension of set-shifting (Huizinga, Dolan, & van der Molan, 2006; Pennington, 1998; van der Sluis et al., 2007). In addition, two of these studies have indicated working memory (the ability to maintain information on line during cognitive processing) to be a separate factor (Huizinga et al., 2006; Pennington, 1998), while a third study deemed this factor 'updating' (replacing previously relevant information with new information relevant to the task; van der Sluis et al. 2007). The evidence for an 'inhibitory control' factor in these studies has been less consistent. While one study isolated an inhibitory control factor (Pennington, 1998), the others found that tasks for which children were asked to inhibit one response in favour of another did not tend to reflect a common latent variable (Huizinga et al., 2006; van der Sluis et al., 2007).

Finally, support for different dimensions of executive function is also provided by the neurological literature. Generally, there is a division of the frontal cortex into the ventro-medial orbitofrontal cortex, the dorsolateral prefrontal cortex and the anterior cingulate cortex. These three areas, though closely associated, also appear to have different responsibilities. The dorsolateral prefrontal cortex appears especially important for spatial planning, working memory and language, generally deemed ‘cold’, abstractive, cognitive aspects of executive function (Zelazo, Qu, & Muller, 2005). The ventromedial prefrontal cortex is more densely connected to subcortical limbic regions and emotional areas of the brain and appears to be more related to social judgement, delay of gratification and reward-based processing. These aspects of executive function are generally thought to be ‘hot’ elements, in that they involve an emotional element (Zelazo et al., 2005). Finally, the anterior cingulate cortex is related to drive, arousal and response selection. It has been especially implicated in tasks that require the resolution of response conflict and interacts with the motor systems (Banfield, Wyland, Macrae, Munte, & Heatherton, 2004; Fuster, 2003; Heyder, Suchan, & Daum, 2004).

Thus, it seems that executive function can be conceptualised as a cognitive system of different skills that act together to allow for effective goal-directed problem-solving (Stuss, Shallice, Alexander, & Picton, 1995). Theoretical discussions of the various elements of executive function generally include working memory, attentional regulation (including inhibitory control, selective and sustained attention), set-shifting or cognitive flexibility and more meta-cognitive skills such as planning, initiation and self-monitoring (Anderson, 2002; Anderson et al., 2002; Banich, 2004; Denckla, 1996; Gioia, Isquith, & Guy, 2001; Hughes et al., 2004; Lezak, 1983; Miyake et al., 2000; Samango-Sprouse, 1999). Although fluency or abstraction is also commonly mentioned, this skill has been found to mature more slowly than others and is therefore less easily assessed in young age groups such as that in the current study (Klenberg et al., 2001).

Tasks for this study were therefore specifically selected on the basis of these factor analysis studies and theoretical models of executive function, with a recognition that more complex tasks will often tax multiple areas of executive function and that the system probably operates in an integrative and interdependent manner (Anderson, 2002; Strauss, Sherman, & Spreen, 2006). The key executive functions considered in this study are briefly described below. To assist the reader in the interpretation of studies reviewed in this chapter, Table 2.1 provides an overview of tasks that are commonly used to assess executive function and the key domains that they are thought to assess.

Table 2.1: Outline of Measures Commonly Used to Assess Executive Function

Task	Construct measured	Description
A-not –B/ search tasks	Working memory/ inhibitory control	Preliminary trials encourage an infant to search for a reward in one location. Following several trials, the object is hidden in an alternative location within view of the infant. After a delay is imposed, young infants generally search in the previously rewarded location.
Card sorting tasks E.g. Wisconsin Card Sorting Task (WCST) and Dimensional Change Card Sort	Set-shifting / mental flexibility Inhibitory control Perseveration	The task involves sorting a set of cards according to different rules. In one condition, the cards are sorted according to one dimension, e.g. according to colour. In the other, they are sorted according to a different dimension (e.g. shape). For younger children, the rule is articulated, but participants must infer the rule according to reward feedback for the WCST.
Continuous performance tests and Go/no-go tests	Inhibitory control Sustained attention Processing speed	Pictures, numbers or words are presented at short intervals on a computer screen. The participant responds to each of these stimuli, except for a pre-selected stimulus that is presented infrequently. The participant must withhold a response to this stimulus. A participant's incorrect responses and response times are recorded on the computer.
Stroop Test E.g. Stroop Tasks	Inhibitory control	The participant must respond to a stimulus such as the word 'green' with a non-prepotent response that generally requires reduced processing speed, e.g. the participant must name the colour of the ink the word 'green' is written in or say 'night' when viewing a picture of a sun.
Memory span tests E.g. Digit span test, sentence span tests or counting span tests	Working memory	Some of these tests, e.g. Digit Span, require the participant to repeat back the cues in sequence or in reverse order. Others, such as the counting span test, involve remembering a set of digits or words, while simultaneously completing a reasoning task.
Fluency tasks	Verbal fluency Design fluency Mental abstraction	These tasks require the participant to generate novel information within some specified parameters. In a verbal fluency task, the participant must generate as many words as possible within a set (animals, for example) in a given time frame. In a design fluency task, the participant must draw patterns within specified grid lines without replicating a previous pattern.

Tower of Hanoi / Tower of London Tasks	Planning/ Problem solving	Coloured disks or beads are arranged on pegs. The participant must transfer disks to a pre-specified goal position. Rules must also be followed (e.g. a large disk cannot be placed on a smaller one), necessitating forethought and sequencing.
Motor sequencing Tasks E.g. hand game, tapping tasks	Inhibitory control Motor fluency	The participant must replicate the actions of the researcher. The researcher then asks the participant to do the opposite of what they are doing, for e.g. In Luria's hand game, the participant must make a fist when the researcher points a finger and vice versa.
Trail Making Tasks	Set-shifting	During the first sequence of this task, the participant connects numbers/letters in sequential order. During the second phase, the participant must switch between numbers and letters (i.e. 1 - A - 2 - B).

2.1.1 Working memory

Working memory has been defined as a system of processing units that allow us to hold goal-related information 'on line' while we process or mentally operate on it (Fuster, 2003; Pennington, 1994; Welsh, 2002; Zoelch, Seitz, & Schumann-Hengsteler, 2005). In accordance with these definitions, working memory is generally thought to be more complex than short term storage components of memory and is generally measured using tasks that require both the storage and the simultaneous utilisation or processing of information (Denckla, 1996).

Although various conceptualizations of the structure of working memory exist, the most widely recognized is that of Baddeley and Hitch (Baddeley, 1986, 1998, 2002), who make the distinction between three key systems: 1) the phonological loop, which retains verbal information for short periods of time, 2) the visual-spatial sketchpad, which operates as a mental drawing board, allowing for the retention of spatial information, and 3) an executive control system that operates on these storage systems, negotiating competing responses and sequencing mental plans. Evidence for the existence of these three separate systems comes from experimental and imaging studies, which indicate that tasks tapping each system can be performed simultaneously (Baddeley, 1986; Baddely, 1996; Cowan, 1997) and activate different regions of the frontal cortex (Jonides & Smith, 1997). In children, the existence of three separate components has also been supported using factor analytic studies (Gathercole, Pickering, Ambridge, & Wearing, 2004).

In general, it seems that this conceptualisation of the central executive is synonymous with executive function as a whole, with tasks such as the division and allocation of attention, inhibitory control and task-switching included in this construct (Zoelch et al., 2005). Indeed, the idea that working memory, by definition of it's limited capacity, necessarily inhibits information, has led some to propose that working memory is sufficient to explain executive function in general (Kimberg et al., 1997; Pennington, 1994). However, such explanations potentially replace one homuncular framework with another, and do not eliminate a need to determine the specific processes that working memory or executive function perform.

2.1.2 Attentional control

Another key aspect of executive function concerns the effective regulation of attention (Ruff & Rothbart, 1996). Studies of attentional networks in the brain indicate that there are 3 principal components of attention (Reuda, Posner, & Rothbart, 2004; Reuda, Posner, & Rothbart, 2005). These include arousal, the most basic form of attention, which is mediated by areas of the hindbrain (Posner, 2000). The second form of attention identified by neurological studies is orienting or selective attention, which involves selecting specific stimuli on which to focus from the myriad sensory stimuli we encounter (Reuda et al., 2004; Reuda et al., 2005). This form of attention is mediated by areas in the midbrain, specifically the striatum, as well as parietal and temporal regions. Finally, researchers refer to executive attention, a more sophisticated form of attention that involves keeping a stimulus in mind and resisting interference, inhibiting responses that are inappropriate and sustaining attention over time (Anderson, 2002). This form of attention appears to rely on communicating regions of the anterior cingulate and the prefrontal cortex (Casey, 2000; Fuster, 2003; Posner, 2000). A key aspect that distinguishes executive attention from other attentional processes is that it involves effortful, volitional control. Aspects of executive attention that were selected for investigation in this study included sustained attention and selective attention (Cohen, Sparling-Cohen, & O'Donnel, 1993; Halperin, 1996; Stuss et al., 1995), as well as inhibitory control, which is described below.

2.1.3 Inhibitory Control

One aspect of executive attention is inhibitory control, or the capacity to control cognition by blocking out irrelevant stimuli (Hughes et al., 2004). Generally, tasks used to assess inhibitory control test the ability to inhibit a prepotent response, interrupt an ongoing response or resist distraction from interference. However, in the context of executive function, inhibition or inhibitory control is often assessed as the conscious suppression of a response that is learned or dominant (Miyake et al., 2000). The importance of inhibitory control for the maintenance of goal-directed behaviour is again illustrated in several case studies of patients with damage to the frontal areas of the brain. In these patients, behaviour is often perseverative (e.g. they will repeat a motoric action, such as shaking hands repeatedly), with irrelevant information often intruding (e.g. while making up stories, the patient will incorporate details about specific objects they are looking at at the time; Duncan, 1986). Inhibitory control may be particularly relevant in the study of disorders of attention and may be a vital first step in allowing us to pause and activate other executive processes, such as working memory, self-regulation and internal dialogue (Barkley, 1997, 1998).

2.1.4 Shifting/Cognitive Flexibility

Set-shifting or cognitive flexibility is also encompassed in the latent construct of executive function. This is the ability to flexibly disengage from a strategy or stimulus that is not appropriate and apply a new one (Barkley, 1997, 1998). Typically, measures of shifting will involve the participant having to replace a learned or typical response with another, often less salient response. In this case, executive control is needed to determine which response is adaptive in the given situation, inhibit the less adaptive response and control responses in accordance with this decision (Ruff & Rothbart, 1996; van der Sluis et al., 2007). Some tests of set-shifting also involve mental abstraction, in that participants must use reward feedback to deduce a new behavioural requirement.

2.1.5 Planning and Self-Monitoring

Planning and problem-solving involve the breakdown and mental dissection of goals into smaller steps and then the re-synthesis of these steps to achieve the goal (Hughes et al., 2004). These processes are required when we have to reach a goal by overcoming obstacles. In order to do this, we must invoke rules or strategies and involve cause and effect principals that are often built up by experience. We also need to consistently evaluate our behaviour based on the goal we are trying to achieve (Bjorklund, 2005). Self-monitoring can include awareness of feedback, checking for mistakes in one’s work and self-pacing (Miller, 2005).

2.2 Development of Executive Function

There is evidence that these different aspects of executive function may develop at varying rates over childhood (Romine & Reynolds, 2005; Welsh &

Pennington, 1988). The emergence of rudimentary executive control can be seen in infancy. By the early age of 9 months, children have developed simple forms of mental representation, as shown by the fact that they can search for a hidden reward in a goal-directed way (Berk, 2006). However, this process can be easily disrupted by placing more obstacles in the child's path. The A-not-B paradigm, originally employed by Piaget (Piaget, 1954), involves repeatedly hiding a reward in an "A' location and then switching the reward, while the child is watching, to a "B" location. After a delay interval of approximately 10 seconds, children below 1 year of age will generally respond by searching at the incorrect A location (Diamond, 2002; Espy, 1999). It has been suggested that children below the age of 1 year generally have difficulty in maintaining a memory trace for extended periods of time (Welsh, Friedman, & Spieker, 2006). However, manipulations of the paradigm have shown that children make the AB error even when looking at the correct "B" location (Diamond, 1985). Thus, it seems that both working memory and inhibitory control may be integral for successful performance. When the A-not-B paradigm is altered by adding more search locations, increasing delay time and adding more barriers to obtaining the reward, children of 2 to 3 years find the switch trial difficult to accomplish correctly. This suggests a progressive improvement in the cognitive mechanisms necessary for successful accomplishment of the task through infancy and early childhood (Espy, 1999; Stahl & Pry, 2005; Zelazo, Reznick, & Spinazzola, 1998).

A further important scaffold for later developments in executive function involves the emergence of symbolic understanding at around 18 months of age (Ruff & Rothbart, 1996). While children of younger ages are able to remember the location of a toy or object, children of around 18 months are able to represent objects as they could be. At around 18 months of age, children also become more self-aware. Thus, they can imagine the consequences of their own actions on their environment. The developments in language and symbolism seen during this period are integral for planning, self-monitoring and higher-level problem solving (Dennis, 1991; Ruff & Rothbart, 1996).

With these developments in mental representation and symbolic thought, children progressively become able to utilize more complex rules to guide goal-directed behaviour. These developments are illustrated in children's ability to solve card-sorting paradigms. For example, Zelazo, Reznick, and Pignon (1995) administered a card-sorting task to children aged 31-33 months. Rules for sorting were based on 'if' statements, such as, "If it is something you can ride, put it here" and, "If it is something that makes music, put it here." However, the researchers also introduced a series of control paradigms to assist children's performance. These included external motivators, memory cues and having children state, rather than enact, sorting rules. The researchers found that children's performance across conditions was similar, apart from the condition where children had only to verbalise the rules, rather than utilising them to sort the cards themselves. In this group, performance was significantly better. Children in other experimental conditions were likely to make perseverative errors by placing cards in a box they had previously used. This suggests that young children are unable to utilise rules or reconcile competing response tendencies effectively to guide behaviour, even though they may be well aware of task requirements.

Important changes occur as children grow. In the Dimensional Change Card Sort (Zelazo et al., 1995), children are required to sort cards according to categories. Cards can be sorted in different ways according to different rules, e.g. shape, colour or size. Using this task, Zelazo and colleagues (Zelazo, 1996; Zelazo et al., 1995) have demonstrated that children are able to progressively sort shapes according to more complex rules. Two year olds, for example, are likely to begin sorting cards according to the correct dimension, but soon after will relapse and sort cards randomly. At approximately 3 years, preschoolers are able to consistently sort cards according to one dimension. When they are asked to sort the cards by a different dimension, however, they are generally unable to do so. As in the former study, children this age were able to state the new rule, but continued to sort by the old one. This is similar to the behaviour of individuals with frontal lobe injuries; they are able to state a rule, but appear unable to apply it (Fernandez-Duque, Baird, & Posner, 2000). At approximately 4 years of age, most children are able to flexibly adopt either rule and apply it when required.

Based on these findings, Zelazo (1996) has suggested that children are progressively able to formulate new rules by combining subrules such as, “If sorting by the shape rule, put the flowers here and the rabbits here,” and “if sorting by the colour rule, put the red ones here and the blue ones here,” into a more complex, embedded rule; “If sorting by shape, put the rabbits here and the flowers here, but if sorting by colour, put the red ones here and the blue ones here.” The gradual integration of these if-then scenarios has implications for higher level planning and problem solving.

Studies using simple paradigms to investigate children’s ability to overcome conflicting impulses have shown that this skill is fairly well developed by 7 years of age, especially for tasks that require the inhibition of motor responses (Reuda et al., 2005; Welsh, 2002). For example, children’s number of correct responses on the tapping task, a task that requires children to override a prepotent motoric response by performing the action that is opposite from the examiner, increases significantly between the ages of 3 and 4. Response latency also becomes much shorter on this task between 5 and 6 years of age (Diamond & Taylor, 1996). Similarly, children’s ability to inhibit their actions on the ‘Simple Simon’ task improves between the ages of 3 and 5 years (Backen Jones, Rothbart, & Posner, 2003; Diamond, 2002). Further developments in more complex forms of inhibition of irrelevant cognitive information continue into late childhood (Zoelch et al., 2005).

With basic inhibitory control, mental representation and rule-based direction of behaviour apparent by the time children enter the classroom, the period of 5 to 7 years represents a rapid growth period for more sophisticated executive function skills. Children of 6 years of age show simple forms of organized searching and planning, with these abilities improving between the ages of 6 and 8 years. For instance, Passler, Isaac, and Hynd (1985) found that the greatest period of developmental change in tasks assessing cognitive inhibition, perseveration and overcoming conflict occurred between 6 and 8 years of age. The group of 6 year olds (age range 5 years, 6 months to 6 years, five months) showed lower performance than the groups of 8, 10 and 12 years olds. Similarly, Welsh et al. (1991) documented significant improvements on a simple variation of the Tower of Hanoi (Simon, 1975) task and in visual search efficiency in a cross-sectional study, such that children’s performance reached the same level as the adult subjects between 5 and 6 years. The researchers surmised that this age corresponds with increased ability to resist distractions and inhibit maladaptive responses.

More recently, Brocki and Bohlin (1999) examined increases in executive function between the ages of 6 and 13. As opposed to reviewing performances in these age groups on a number of different tests, these authors first completed a factor analysis of their results and evaluated age-related changes for 1) a disinhibition factor, comprising components of two go-no-go type tasks, 2) a speed/arousal factor, comprising reaction time and failure to respond on these tasks, and 3) a working memory/fluency factor, consisting of spatial and verbal working memory measures and a variation of the Stroop Task (Golden, 1978). Analyses showed that the greatest improvement in children's performance on the speed and working memory factors occurred between the ages of 6 and 7 years.

A recent meta-analysis (Romine & Reynolds, 2005) summarised 7 studies examining age related changes in executive abilities in children of 5 to 17 years. This study showed that the greatest increases in ability occurred between the ages of 5 to 8 years, with an average effect size (Cohen's *d*) of 1.17 for age-related changes in performance across measures of planning, fluency, inhibition and set-shifting in this age bracket. Another review (Anderson, 2002) highlighted early to middle childhood as representing a period of rapid improvement in the ability to control attention, process information fluently and flexibly shift between dimensions.

Therefore, several studies converge to suggest that, building on the development of mental representation, simple inhibitory control, symbolic understanding and the appreciation of complex if-then scenarios, the 5-7 year shift represents a major period of development in executive function. Such findings suggest that this will also be a time when developmental assessment is likely to reveal increasing individual differences in the development of these key executive skills and their manifestation as children enter the school environment.

2.3 Neurological Development in Relation to Executive Function in Children

Developmental changes in executive control through early and middle childhood are thought to reflect underlying changes in the development and organisation of the brain (Luciana, 2003b). Several researchers have highlighted synaptogenesis and synaptic pruning in the prefrontal cortex as being important for the development of executive function (Huttenlocher & Dabholkar, 1997). Consistent with this point of view, many researchers continue to cite the protracted development of the prefrontal cortex as being the principle mechanism for the maturation of executive function (Conklin, Luciana, Hooper, & Yarger, 2007). However, there is growing recognition that it is unlikely that specific cognitive functions map directly to single regions of the brain. Indeed, the complexity of prefrontal cortex connections to and from subcortical and cortical areas lends support to the notion that these areas work in concert, with bottom-up information reaching the prefrontal cortex via subcortical regions and the frontal areas providing top-down feedback and control over other areas (Carpenter, Just, & Reichle, 2000; Elliot, 2003; Heyder et al., 2004; Zelazo & Muller, 2002).

In support of this view, lesions or degeneration of other subcortical and cortical areas often result in similar deficits to those reported with prefrontal lesions (Elliot, 2003; Heyder et al., 2004). Lesions to the striatal area have been shown to disrupt spatial working memory in monkeys during childhood, while lesions to the prefrontal cortex do not appear to affect performance until young adulthood (Goldman, 1972, cited in Luciana, 2003a). Studies of children with a diagnosis of ADHD have also documented smaller caudate volumes in these children, with smaller volumes associated with lower performance on a measure of inhibitory control (Casey et al., 1997; Krain & Castellanos, 2006). Finally, neuroimaging studies have found diffuse activation including areas of the parietal and motor areas during the completion of executive tasks (Carpenter et al., 2000; Smith & Jonides, 1999). These findings suggest that connections between subcortical and cortical neural systems are particularly important for the effective development of working memory and planning skills and that key executive skills that are mediated by the prefrontal regions during adulthood may be more related to subcortical function earlier in development. When considering the growth of the brain in relation to executive function, it is therefore important to consider the brain as interconnected, with fibres between the prefrontal cortex and subcortical nuclei operating as feedback loops.

During early and middle childhood, there are significant changes in the organisation and structure of the brain. Specifically, there are changes in the volumes of cortical and subcortical grey and white matter in different areas (Giedd et al., 1996; Romine & Reynolds, 2005). These changes are brought about by synaptogenesis, synaptic pruning, myelination, axonal growth and dendritic branching (Conklin et al., 2007; Diamond, 2002; Fuster, 2002; Goldman-Rakic, 1987), with associated changes in glucose and neuroreceptor levels (Romine & Reynolds, 2005). In terms of synaptogenesis and pruning, studies of monkeys have shown that their ability to perform the A-not-B task corresponds with a peak in synaptic density in the principal sulcus of the dorsolateral prefrontal cortex, suggesting that the development of these synapses and subsequent elimination of unnecessary connections may underlie developments in spatial working memory (Diamond & Goldman-Rakic, 1986; Goldman-Rakic, 1987). The same researchers have shown similar findings for a task that involves inhibitory control of the tendency to reach according to line of sight in infants. Similarly, in older children, reduced volumes in key fronto-striatal grey matter regions, including the prefrontal cortex and basal ganglia, have been associated with lower performance on tests of inhibitory control (Casey et al., 1997).

Importantly, there is increased connectivity to and from the frontal regions through childhood. Myelination of cortical tracts continues for many years after birth. For example, myelination of the corpus callosum, which links the hemispheres of the brain, accelerates between 3 and 6 years of age (Kagan, Herschkowitz, & Herschkowitz, 2005), while the density of white matter in the internal capsule increases steadily between the ages of 4 and 17 (Paus et al., 1999). Areas such as the internal capsule, thalamus and basal ganglia also show age-related increases in the extent of white matter development (Barnea-Goraly et al., 2005; Tomas et al., 1999). Temporally, the frontal areas of the brain are some of the last to myelinate (Diamond, 2002; Fuster, 2002; Stuss, 1992), perhaps making connections between these regions more vulnerable to long-term disruption. In support of the importance of myelin in the development of executive function, MRI studies show a correlation between working memory capacity and myelination in children of older ages (Nagy, Westerberg, & Klingberg, 2004). With increased interconnectivity, functional MRI, Positive Emission Temography and electroencephalogram (EEG) studies also show a more focal activation of the brain areas specific to tasks, associated with better performance on measures of selective attention and inhibitory control (Bell & Fox, 1992; Durston & Casey, 2006; Konrad et al., 2005; Reuda et al., 2005). This suggests that it is the integrated connectivity of neural circuits that increases the efficiency of cognitive control on these tasks. Development of these communicative networks and faster transmission within the brain is likely to affect the development of executive function, with damage early in life likely to disrupt subcortical-cortical connectivity and to have ongoing repercussions for the organisation of goal-related activity (Luciana, 2003b).

2.4 The Role of Executive Function in Academic Achievement

Developmental changes in executive function are also thought to scaffold learning and have been shown to be integral for achievement in basic academic domains (Blair & Razza, 2007). Conceptually, mathematical performance should rely on key functions of working memory and central executive control to store, manipulate and integrate information and concepts from long-term memory, strategise and focus on salient information. Supporting evidence for relationships between mathematics achievement and executive function comes from studies of children with learning disabilities, as well as a few studies that have examined relationships between executive function and academic achievement in normative samples. These studies have generally been modelled on a tripartite view of working memory (Baddeley, 1986), and therefore divide working memory measures according to whether they reflect processes of the phonological loop, the visuo-spatial sketch pad or the central executive.

Using such models, studies have been consistent in showing that children with difficulties in mathematics also have more difficulty completing tasks that involve central executive processes (Bull & Scerif, 2001; D'Amico & Guarnela, 2005; Espy et al., 2004; Geary, Hoard, Byrd-Cracen, Nugent, & Numtee, 2007; Geary, Hoard, Byrd-Craven, & DeSoto, 2004; van der Sluis, de Jong, & Van der Leij, 2004). For example, D’Amico and Guarnela (2005) showed that children who were performing poorly in mathematics, but not reading, also performed poorly on complex span tasks such as the backward Digit Span task and Trail Making Task (Reitan, 1958). However, these researchers also showed that difficulties in manipulating visuo-spatial information were more prevalent in this group. In contrast, the children characterised by impaired mathematics ability did not show difficulty on tasks designed to tap the short-term phonological loop only (e.g. repetition of non-words). Such findings suggest that children who struggle in mathematics may have greater difficulty in storing spatial information in working memory and in manipulating and processing information in accordance with a goal.

Another study (Geary et al., 2004) showed that developments in working memory are related to the strategies that children employ when completing arithmetic problems. Less advanced mathematical strategies, such as counting on fingers, were employed by children who were poorer at maths. These children also had lower working memory spans, as measured by a counting span task. In older children, higher working memory spans were correlated with the tendency to use a more advanced strategy, decomposition, to solve more complex mathematical problems (e.g. to solve the problem 11 x 16, these children would break the problem into subcomponents, 10 x 16 + 16), while those who had poorer working memory spans were likely to rely on guessing.

Further studies have shown impairments in specific elements of executive function in children with difficulties in mathematics. Two studies, for example, have found that children with mathematics difficulties have difficulties in inhibitory control and shifting (Bull & Scerif, 2001; van der Sluis et al., 2004). In one of these studies, children were selected into one of four groups according to whether they had difficulties in arithmetic, reading or both (defined as being 15 months behind achievement level expected for their age). Tasks were designed to tap inhibitory control and set-shifting ability while controlling for processing speed. This study showed that children with mathematics or mathematics and reading difficulties were less likely to be able to suppress prepotent responses and had difficulty when required to switch flexibly between rules and inhibit a prepotent response simultaneously. Poor readers, however, performed at a level equivalent to children of average achievement on the measures of inhibitory control and set-shifting.

There is less robust evidence for the role of executive function in reading achievement, with findings varying according to tests employed and groups studied (de Jong, 1998; Jeffries & Everatt, 2004; Pennington, Groisser, & Welsh, 1993). Some studies have suggested that working memory capacity is related to reading ability. For example, de Jong (1998) found that children who were at least 2 years behind in their reading showed lower span levels than an age-matched control group on tests of phonological short term memory and working memory. This study also controlled for processing speed. Similarly, Jeffries and Everatt (2004) found that children with dyslexia obtained lower scores on measures selected to tap the phonological loop function of working memory (e.g. digit recall), and central executive function (e.g. backward digit recall), but showed no differences to an average-achieving control group in their ability on tasks designed to tap visuo-spatial processing (e.g. block recall). It must be noted that the central executive measures on which children with dyslexia did under-perform were language-based measures, suggesting that difficulties with reading may relate more to phonological processing difficulties than to difficulties in executive function per se.

While there is continued debate as to whether children with reading impairments have difficulties that are confined to phonological processing or whether a broader executive deficit is applicable, it seems that when language comprehension is required, central executive processes are probably integral. A meta analysis of 77 studies and 6179 participants showed that correlations between working memory and language comprehension scores were high for most studies, with studies that had employed measures capturing both the storage and processing demands of working memory finding larger effect sizes (r=0.09-0.73) than those that measured verbal or spatial storage alone (0.08-0.55; Daneman & Merikle, 1996). Conceptually, the constant updating and integration of information required for language comprehension would be expected to place high demands on executive resources.

Together, these studies indicate that the construct of executive function offers us much promise in being able to identify children who may be at risk for difficulties in key areas of academic achievement. This may be especially true in the domain of mathematics, where the challenge of drawing on learned strategies and flexibly applying them while confronting novel information is likely to place substantial demands on working memory and the flexible processing of information.

Consequently, differences in executive function may well help researchers to understand the neuropsychological difficulties associated with preterm birth and identify which of these children are likely to show poor academic development.

This introduction to executive function has suggested that it appears to be a multidimensional construct, incorporating skills such as holding information in mind and conducting mental operations on it simultaneously, exercising attentional control, planning and strategising, initiating activity, monitoring and evaluating action. The period of 5 to 7 years represents an important period of development of these skills. Rudimentary abilities such as the ability to represent information in working memory, symbolic thought, the regulation of attention and the ability to hold several rules in mind and utilise them flexibly have been shown to be in place by this age, with fluency, metacognition and more complex goal-related processing continuing to develop. Such skills are integral for children's successful transition to a classroom environment and for the successful acquisition of reading, comprehension and mathematical skills.

Unfortunately, there continue to be a number of issues surrounding the concept of executive function. Many of these issues centre around measurement and construct validity. Essentially, tasks used to measure executive function are complex and multi-dimensional, incorporating various other domains of cognition. Thus, the separation of the executive from the non-executive processes is difficult, with the differentiation of different executive processes perhaps being more difficult still (Fletcher et al., 1996; Frith, Gallagher, & Maguire, 2004). Added to this difficulty is the fact that executive function is dynamic, as is clear from the above review of its development. Specific measures of executive capacities will be more or less appropriate with different age groups, according to the stage of development of the child and the nature of tasks employed.

It is also important to note that performance on tasks in a laboratory setting may not be reflective of children's executive function in other contexts. Volition and goal formation are important components of executive function, so the attractiveness of the task and the child's appreciation of the goal will be important in influencing the strategies they employ and their motivation to achieve. Thus, evaluation of performance in different settings and from different observers will be a necessary compliment to information from task performance alone. Similarly, although overall performance on these tasks may be a useful measure of task success, it must be repeated that these measures are a proxy for underlying processes (e.g. the use of strategy, error-correction and sustained attention). Thus, the use of behavioural observation in conjunction with task measures may help to clarify whether task performance is related to the executive strategies that children employ.

Finally, there has and continues to be much debate around the relationship between executive function and intelligence. Certainly, the relationship between working memory and 'fluid' measures of intelligence, which require reasoning and problem solving, appears strong (Carpenter, Just, & Shell, 1990; Fry & Hale, 2000). However, in the context of very preterm birth, the utility of executive function and problem-solving measures lies in the question of whether they are able to offer any more information to teachers, psychologists and interventionists over and above what is already available from standardised testing. While there is large body of literature suggesting a lower distribution of IQ scores in children born very preterm, questions about the specificity of these difficulties remain. Evidence for a relationship between academic achievement and executive function implies that, despite the aforementioned limitations in measurement, observed task measures have external validity in being able to identify the specific areas of cognition that may be challenging for children born very preterm.

Chapter 3

Executive Function in Children Born Very Preterm

Existing follow up research with children born very preterm has provided a global description of the nature of their cognitive deficits, using general developmental measures such as the *Bayley Scales of Infant Development* (BSID; Bayley, 1969, 1993) and the *WISC* (Wechsler, 1967, 1974, 1989, 1991, 2003). These tests do not provide for the separate measurement of processes such as attention, planning, strategy induction or perseverative behaviour, difficulties with which are often anecdotally reported by psychologists as characterising children who struggle to achieve in a learning environment (Naglieri, 1990). Thus, limited information is available concerning the specific neuropsychological deficits that may account for higher rates of cognitive and educational delay among children born very preterm (Rose & Feldman, 1996). It is essential that psychologists now move beyond generalised IQ testing by incorporating new knowledge of the development of metacognition and executive function into follow up studies (Aylward, 2002). In recognition of this, a small number of researchers have begun to investigate relationships between very preterm birth and individual cognitive processes.

Table 3.1 provides an overview of studies that have examined executive function in groups of children born preterm, describing the sampling frames, recruitment and retention rates, year of birth, measures, effect sizes and strengths and limitations of the various studies. These studies were accessed via searches in the PsychInfo, PubMed and Web of Science databases using combinations of the following key words: preterm, LBW, VLBW, executive function, working memory, attention, impulse control, neuropsych*. Where statistical information allowed, Cohen's *d* effect sizes were calculated. Specific aspects of executive function that have been studied are considered below.

3.1 Working Memory in Children Born Very Preterm

Memory is one of the most extensively researched areas of cognitive function in children born very preterm. However, studies of memory have yielded contrasting findings (Briscoe et al., 1998; Briscoe, Gathercole, & Marlow, 2001; Dewey, Crawford, Creighton, & Suave, 2000; Naberhaus et al., 2007; Rose & Feldman, 2000). Some studies suggest discrepancies in the mean scores of children born very preterm (Dewey et al., 2000; Naberhaus et al., 2007; Rose & Feldman, 2000), while others indicate that global difficulties in memory may be restricted to small subset of children concomitant with lower IQ and language delay (Briscoe et al., 1998, 2001). One reason for these contrasting findings may be that the above studies have treated memory as a broad construct, with average scores across memory subtests reported. There is now increasing evidence that children born very preterm may be more susceptible to impairments in specific aspects of memory that rely more heavily on the utilisation of executive resources. These areas include spatial and verbal working memory.

Spatial working memory has been studied in younger children born very preterm using tasks that require the retrieval of a hidden object from a location after a period of delay (Caravale, Tozzi, Albino, & Vicari, 2005; Espy et al., 2002; Vicari et al., 2004; Woodward, 2005). For example, Espy et al. (2002) assessed working memory in a group of 29 toddlers born preterm (<37 weeks GA, <1900g) and 29 toddlers born full term. A spatial alternation task required children to alternate searching between two locations in order to retrieve a reward. As such, the task assessed the ability to remember the position of the reward on the previous trial and use this mental representation to guide behaviour. Significant between group differences were found on this task, with children in the preterm group correctly retrieving the reward on 40% of trials compared to children in the full-term group, who correctly retrieved the reward on 50% of trials ($p<0.01$). Children in the preterm group also showed a perseverative tendency to return to the previous search location more often than those in the full term group ($p<0.05$). This suggests a failure to effectively encode, retrieve or act on information about the new object location.

Further studies using similar paradigms have identified deficits in spatial working memory in young children born preterm even after controlling for IQ and neurological abnormality (Caravale et al., 2005; Vicari et al., 2004). Both of these studies employed a task that required children to remember the location of an object placed under one of a series of cups. Cups were arranged in different ways – horizontally, diagonally and in an L-shape - over different trials. Across both studies, children born <34 weeks gestation performed less well on this task when compared with a group of same-age peers born full term ($p<0.05$). In addition, Vicari et al. (2004) showed that there was an effect of delay time. Children in the very preterm group showed performances similar to those in the full term group when a 1 second delay was imposed between hiding and searching, but correctly retrieved the toy on fewer trials at delay intervals of 5 and 10 seconds. Children were recruited from follow-up clinics, raising questions about the generalisability of findings to the wider population of children born very preterm. Nonetheless, findings support those of Espy et al. (2002) in suggesting that children born very preterm may have difficulty retaining a memory trace for spatial information, especially over longer time intervals. They also support findings from previous research with the present cohort, which demonstrated deficits in performance on a spatial working memory task at 2 years of age, adjusted for prematurity (Woodward, 2005).

Therefore, working memory for spatial location appears to be a specific domain of memory that presents challenges for young children born very preterm. Effect sizes for the above studies have been moderate to large, suggesting that this particular area of cognition is in further need of study in large, heterogeneous groups of children. Although two studies (Matthews, Ellis, & Nelson, 1996; Wilcox, Nadel, & Rosser, 1996) have failed to replicate this finding of impaired memory for object location in young children born very preterm, these studies were conducted with small samples of children of older gestation and birthweight (<2500g), a factor that shall be considered in the following chapter.

Difficulties in spatial working memory have also been found in older children born very preterm using spatial span and spatial sequencing memory tasks (Bohm, Smedler, & Forrsberg, 2004; Curtis, Lindecke, Georgieff, & Nelson, 2002; Kulseng et al., 2006; Luciana, Lindeke, Georgieff, Mills, & Nelson, 1999; Taylor et al., 2004). Luciana et al. (1999) employed the Cambridge Neuropsychological Testing Automated Battery (CANTAB; Fray, Robbins, & Sahakian, 1996) to test spatial span and spatial working memory in children who had been admitted to the NICU. The CANTAB is a series of computerised tasks, which are sensitive to injury in the temporal and dorsolateral areas in the brain. The study group comprised 40 7-9 year old children who were born <40 weeks GA. Of these, 22 were born <1500g and 17 <2500g. An age-matched control group of 90 children also completed the tasks. Children who had been in the NICU achieved a mean spatial memory span that was lower than that of their same-age peers ($p<0.01$). They also made more errors and showed less ability to effectively strategise on the spatial working memory span task ($p<0.05$). These findings were replicated in the same sample of children at 10-14 years of age (Curtis et al., 2002). However, given the heterogeneity of medical experiences in this sample, these findings require further replication in samples restricted to children born very preterm.

Fewer studies have examined verbal working memory in children born very preterm. Studies that have examined this domain have reported mixed findings. To date, the most commonly used measure of verbal memory is the Digit Span test. Of the studies reviewed, three (Anderson, Doyle, & Victorian Infant Collaborative Study Group, 2004; Isaacs et al., 2000; Rose & Feldman, 2000) reported that children born very preterm performed less well on this measure than children born full term. The first study compared 298 children born extremely preterm (<28 weeks GA/<1000g) and 223 children born at term age when they were 8-9 years of age. Groups were matched for gender, SES and expected date of delivery (Anderson et al., 2004). Children received an overall verbal span score based on their ability to repeat back a series of numbers in forwards, then backwards, sequence. The effect size for the group difference in digit span score was 0.35 and therefore small (Cohen, 1988). Of note, this sample was made up of children born ELBW, potentially making these children more vulnerable to impairment. In contrast to these findings, three other studies including children born VLBW have reported no discrepancies in digit span relative to full term control groups (Bohm et al., 2004; Korkman, Liikanen, & Fellman, 1996; Rushe et al., 2001).

While differences in these findings for digit span tasks may be due to several factors, one particularly relevant factor may be that most studies have failed to distinguish between differences in the recall of sequences of numbers in backwards or forwards order. Instead, researchers have summed scores across both parts of the task to produce a composite indicator of performance. Recalling a series of numbers in backwards order conceivably requires more executive control, in that one needs to inhibit the tendency to repeat the forwards sequence, and manipulate numbers in working memory in order to successfully recall and repeat them. Failure to consider the influence of these increased executive requirements for backward span trials is important because disparities in the performance of children born very preterm on memory tasks appear to increase as these tasks become more demanding on working memory (Curtis et al., 2002; de Haan, Bauer, Georgieff, & Nelson, 2000; Luciana et al., 1999; Rose & Feldman, 1996). For example, de Haan et al. (2000) examined memory for sequences of modelled actions in children aged 19 months, corrected for prematurity. The sample was stratified into 3 groups according to gestational age at birth: 1) very preterm (27-34 weeks), 2) preterm (35-37 weeks) and 3) full term (38-42 weeks), with 16 children in each group. Under both immediate recall and delayed recall conditions, groups performed comparably in terms of the specific actions children recalled. However, children in the very preterm group were less likely to perform the actions in the correct sequence when compared to the full term group ($p<0.05$). These findings suggest that sequenced information may pose more of a challenge for children born very preterm, perhaps due to the increased taxation on working memory required for the correct ordering of events. Other studies have also indicated that the effect sizes for group differences in spatial working memory increase as a function of increased cognitive load (Curtis et al., 2002; Luciana et al., 1999; Vicari et al., 2004).

Only one study has examined the relative performance of children born very preterm on forward and backward trials of a digit span task. The study found that scores on the Digit Span subtest of the WISC-III were significantly different, but that this difference was predominantly driven by lower scores on the backwards sequence trials of the task (Isaacs et al., 2000). Findings from this study are not generalisable as the group of children born very preterm was small (n=11) and selected from a larger sample. However, they do raise questions as to whether, in accordance with the findings from spatial span tests in children born very preterm, increasing the executive load on verbal working memory would affect children's task performance.

3.2 Planning and Problem Solving in Children Born Very Preterm

Planning and strategising is a second area of executive function that has been examined in children born very preterm. Relative to groups of children born full term, children born very preterm show lower performance on complex planning and strategising tasks. Such tasks include the Tower of Hanoi (Harvey, O' Callaghan, & Mohay, 1999; Marlow et al., 2007; Mellier & Fessard, 1998; Wall, 1996), Tower of London (Anderson et al., 2004; Luciana et al., 1999; Shallice, 1982; Taylor et al., 2004) and Rey Complex Figure (Anderson et al., 2004; Osterrieth, 1993; Taylor et al., 2004).

In younger age groups, two studies (Harvey et al., 1999; Marlow et al., 2007) have reported poorer performance on tower tasks. Of note, both of these studies have been restricted to children born extremely preterm (<28 weeks GA), making it difficult to generalise findings to children born very preterm. In the study by Harvey et al. (1999), the median score of children born extremely preterm on the Tower of Hanoi at age 5 years was 0, relative to a median of 4 amongst children born full term. In this study, a score of 0 indicated that children were unable to complete the task in less than 10 moves after 6 successive trials. Thus, difficulties on this planning task persisted despite several opportunities for children born extremely preterm to correct the errors they had made during previous attempts at the task.

Difficulties on planning tasks have also been found in older children born very preterm. For example, in a sample of adolescents ranging in age from 14-21 years, Taylor et al. (2004) found that children born VLBW (<1500g) were less likely to be successful in solving a Tower of London-like task in the prescribed number of moves than a full term comparison group ($p<0.05$). The VLBW group took less time to plan their initial moves and longer to complete the task. This suggests that they were initially impulsive and failed to strategise, but then took longer to process the task. Similarly, Mellier and Fessard (1998) found that 12 adolescents born <33 weeks GA were less likely than a group of full term peers to achieve the Tower of Hanoi task in the optimal number of moves. Instead, they tended to have to self-correct and complete the task in a greater number of moves.

Collectively, these studies are consistent in suggesting impairments in the ability to internally generate plans or options and assess their implementation across both younger and older children born very preterm. More in-depth analysis of the reasons for failure on these tasks suggests that children born very preterm may also have difficulty self-correcting or monitoring their own performance, more difficulty processing the task requirements and more difficulty inhibiting incorrect move responses.

3.3 Executive Attention in Children born Very Preterm

Attention is another area in which children born very preterm may experience difficulties. Early researchers described children born preterm as being inattentive and restless (Mellier & Fessard, 1998). In keeping with these early observations, a number of studies employing checklist measures, such as the *Child Behaviour Checklist* (Achenbach, 1991) and the *Connor's Ratings Scales* (Connors, 1997), have reported higher incidences of attention difficulties amongst children born preterm (Cooke, 2004; Delobel-Ayoub et al., 1996; Foulder-Hughes & Cooke, 2003; Klebanov, Brooks-Gunn, & McCormick, 1994a; Schothorst & van Engeland, 1996; Winders-Davis, 2003). These studies have predominantly relied on parent report (Delobel-Ayoub et al., 1996), but a few have also used teachers (Foulder-Hughes &

Cooke, 2003; Klebanov et al., 1994a) or participants themselves (Cooke, 2004) as informants. Despite these consistent reports of inattentiveness using checklist measures, as well as the high rates of ADHD reported in children born very preterm (Bhutta et al., 2002; Botting et al., 1997; Mick, Biederman, Prince, Fischer, & Faroane, 2002), few studies have examined different components of attention using laboratory-based assessment measures.

Inhibitory Control in Children Born Very Preterm. Studies employing laboratory-based measures of inhibitory control have produced mixed results. Some support for a deficit in inhibitory control comes from studies that have shown that early school-aged children born preterm make more errors or are slower to respond on measures of motor inhibition, such as Luria's hand game (Bohm et al., 2002; Bohm et al., 2004; Harvey et al., 1999). One exception is a study that compared a group of 138 children born <1000g and <28 weeks GA to 61 children born full term on tests of motor inhibition at age 5 years (Esbjorn, Hansen, Greisen, & Mortenson, 2006). Tests included 1) a knock and tap test similar to Luria's hand game, and 2) an assessment of how long children could stand still and keep their eyes shut while distracting aural stimuli were presented. There were no significant group differences on these tasks. However, the study was limited in that very few participants from the overall sample completed these tests, introducing the possibility of self-selection bias.

In contrast to tasks assessing motor inhibition, fewer studies have found differences when there is less demand on motor skills and when tests have been administered to older children. Studies using the Stroop task (Golden, 1978) have reported no significant differences between the performance of children born very preterm and children born full term (Elgen, Lundervold, & Sommerfelt, 2004; Mellier & Fessard, 1998). The Stroop task is advantageous in that it requires the inhibition of a cognitive response with no requirement of motoric control. One possibility for differences in study findings is that, as motorist inhibitory control is a relatively well-developed skill in non-clinical samples of children by 6-8 years, impaired performance in younger children born very preterm may reflect a delay in the development of inhibitory control, with a relative ‘catch up’ at later ages.

Selective and Sustained Attention in Children Born Very Preterm. Studies of younger children born very preterm have also shown that they obtain lower scores on search tasks that require them to identify a series of visual targets or pictures amidst an array of distracters (Caravale et al., 2005; Pasman et al., 1998; Vicari et al., 2004). One reason for this may be that they are less likely to inhibit attention to distracter items and selectively attend to stimuli. However, a more detailed analysis of visual search performance amongst children born extremely preterm showed that they did not make more errors of commission (i.e. nominating incorrect targets), but instead made more errors of omission (i.e. failing to nominate correct target items) and spent more time off-task (Marlow et al., 2007) . This suggests that difficulties on such tasks may relate to impairments in the sustained and focussed aspects of attention, as opposed to difficulties in inhibitory control.

Elgen et al. (2004) have also argued that children born preterm are likely to show deficits in the sustained aspects of attention, rather than difficulties in inhibitory control. In addition to the Stroop Colour-Word task, this study included the Continuous Performance Task (Connors, 1995) to assess inhibitory control, sustained attention and reaction speed. The performance of children born very preterm (<2000g, <32 weeks GA) was compared to that of full-term peers at age 11 years. There were no between group differences in inhibitory control, as assessed by the Continuous Performance and the Stroop tasks. Instead, children in the preterm group were more likely to make errors of omission (failures to respond; $p<0.05$), suggesting greater difficulties in sustaining attention or maintaining vigilance.

One other study has suggested difficulties in both sustained attention and inhibitory control amongst children born very preterm (<34 weeks GA, n=64; Katz et al., 1996). This study included children born very preterm and children born full term (n=40) at age 6-8 years. Findings showed that both errors of commission (incorrectly responding to a non-target stimulus) and errors of omission (failing to respond to a target stimulus) were significantly higher in the group of children born very preterm ($p<0.05$). One factor that may have influenced the likelihood of detecting differences for both components of attention in this study is the fact that the continuous performance task administered was relatively complex. As opposed to merely inhibiting the response to a stimulus, children were required to respond to the target letter “X” when the previous stimulus was an “A.” Thus, this task requires a high degree of monitoring and updating of working memory in comparison to typical continuous performance task measures. Again, this may suggest that children born very preterm are more likely to show poor performance when demands on working memory are high.

Therefore, the weight of research evidence suggests that children born very preterm show difficulties in the executive aspects of attention. However, there is less agreement as to whether these difficulties are related to impulsive behaviour and a failure to inhibit motor responses or whether they reflect lapses in vigilance and difficulty in sustaining attention. This is a complex issue, in that inhibitory control has been argued to support sustained attention (Hughes et al., 2004) and researchers sometimes report overall performance scores on tasks, without separating these two attentional components (Bayless & Stevenson, 2006). Such inconsistencies in the literature suggest a need for further research to determine which specific aspects of executive control are affected by very preterm birth and whether differences in findings may be related to changes in development across time.

3.4 Set-shifting and Attentional Flexibility in Children Born Very Preterm

Set-shifting or attentional flexibility is another aspect of executive function that has been of some interest in studies of children born very preterm. The measurement and conceptualisation of set-shifting has varied across studies. Due to the complexity of set-shifting tasks for older children and adults, researchers often develop novel paradigms in order to examine this skill in younger children. For example, at preschool age, Espy et al. (2002) assessed a group of children born preterm (<37 weeks GA) and full term on a spatial reversal task. The task required children to correctly search a location for four trials and then flexibly switch location after four trials, when the reward was hidden in a different location. Thus, children need to deduce the rule for searching and flexibly apply it. Twenty trials were administered, the dependent variable being the number of trials during which the child correctly retrieved the reward. There were no significant differences in the performance of children born very preterm and full term on this task. This finding has been replicated using the same task with a different group of children born preterm (Mean GA=30 weeks) at age 6 years (Landry, Miller-Loncar, Smith, & Swank, 2002). The absence of group differences in these studies may suggest a relative sparing of set-shifting ability in young children born very preterm, although children in these studies were of low medical risk, potentially making them less vulnerable to impairments.

In line with the findings above, none of the researchers who have employed the CANTAB to study executive performance in older children born preterm have reported lower scores on the set-shifting task, relative to groups of full term children (Curtis et al., 2002; Luciana et al., 1999; Taylor et al., 2004). Similar to the Spatial

Reversal task described by Espy et al. (2002), this task requires participants to switch their responses to a visual stimulus based on reward feedback, thereby assessing children’s ability to deduce rules and flexibility shift response sets.

However, other studies using set-shifting tasks that require children to alternate between responding to numbers and letters (Kulseng et al., 2006; Rushe et al., 2001) or colours and shapes (Bayless & Stevenson, 2006; Bohm et al., 2002; Bohm et al., 2004; Taylor et al., 2004) have reported poorer performance in children born very preterm relative to children born full term. One of these studies examined a sample of very preterm children (<32 weeks GA) and full term children aged 6-13 years on a range of executive function measures (Bayless & Stevenson, 2006). Children in the very preterm group showed the largest performance discrepancy on a test of set-shifting from the Test of Everyday Attention (TEA-Ch; Manly, Robertson, Anderson, & Nimmo-Smith, 1999). The TEA-Ch task involves continually switching between counting stimuli on a computer screen in an upwards or downwards fashion. Interestingly, this measure of executive function was the only domain of executive function tested by Bayless and Stevenson (2006) in which between-group differences remained significant after controlling for the effect of IQ.

The pronounced differences in findings for studies that have examined set-shifting in children born very preterm are difficult to explain, especially given that there is no apparent developmental trend in terms of age. One possible factor that may help to account for discrepancies across these study findings is that both Espy’s set-shifting task and the CANTAB involve continuous reward feedback, thereby perhaps reminding children of the task requirements and decreasing the load on working memory. This continuous environmental input may also mean that children who are generally stimulus-bound, and poor at regulating their own motivation and attention, receive supportive external scaffolding from task rewards, thereby decreasing demands on working memory. Interestingly, while studies employing the Wisconsin Card Sorting task (Heaton, Thompson, & Gomez, 1999) with adult samples have generally shown that this task is associated with the dorsolateral regions of the prefrontal cortex, reward-based responses have been ascribed to ventromedial circuits, thereby suggesting differences in the neural areas that these tasks may tax (Espy et al., 2002; Noble, McCandliss, & Farah, 2007). Differences in the neural circuits that these tasks tap also support the idea that the set-shifting tasks employed across studies may tap different executive requirements.

3.5 Behavioural Measures of Executive Function

An important limitation in terms of establishing the ecological validity of executive function measures is that very few researchers have triangulated task performance with third party reports or observational ratings. Apart from the above-reported studies that have used checklist measures to examine attention and hyperactivity in children born very preterm, a small number of studies have used behavioural report and behavioural observation to assess self-regulation and self-monitoring in children born very preterm. Anderson et al. (2004) found that parents of children born ELBW (<1000g) were more likely to rate them as having less capacity to monitor their own actions and as being less likely to initiate activity of their own accord. Parents also reported difficulties in planning and working memory amongst children born very preterm, supporting findings from laboratory-based measures. Similarly, Bohm et al. (2004) designed a behavioural rating scale to assess levels of distractibility, activity and mental effort in their study of children born <1500g. While no between group differences were found in levels of activity or distractibility, examiners were more likely to rate children born very preterm as being less motivated or curious than term-born control children ($p<0.05$).

3.6 Associations between Executive Function and Academic Achievement in Children Born Very Preterm

In terms of the implications of these executive function impairments for the transition to schooling, there is some evidence to suggest that early attention and information processing may be related to later achievement in children born very preterm (Lawson & Ruff, 2004; Rose, 1983). Studies by Rose, Feldman, and colleagues (Rose, 1983; Rose, Feldman, & Wallace, 1988; Rose, Feldman, Wallace, & McCarton, 1989) have suggested delays or deficits in the development of information processing, memory and attention in groups of children born VBLW. In these studies, children born VLBW (<1500g) and children born full term were administered habituation tests. These tests measured preference for a novel stimulus by presenting a picture, shape or object for a varying time interval and then pairing it with a new, unfamiliar stimulus. The extent to which children showed a novelty preference for the new stimulus, measured by the time they spent looking at the new stimulus relative to the old, was recorded as the dependent variable for each task. The first study (1983) was conducted with children at 6 months and 1 year (corrected for prematurity). Results showed that children born VLBW (n=20) had to be familiarised with the novel stimulus for a longer period of time than children born full term (n=20) before they showed a novelty preference ($p<0.01$). This suggests that the infants were inattentive or slower to process information at these ages. The second of these studies (1988) was conducted with larger sample of VLBW (n=63) and full term (n=46) children at 6, 7, and 8 months of age. Results corroborated earlier findings: children in the very preterm group did not show a novelty preference before 8 months of age, while their full term peers showed a novelty preference across all ages.

In a series of follow-up studies, Rose and colleagues (Rose, Feldman, Futterweit, & Jankowski, 1997; Rose, Feldman, & Wallace, 1992; Rose et al., 1989) showed that there were significant correlations (r = 0.37-0.65) between performance on the recognition tasks they administered at 7 months of age and later achievement on standardised cognitive tests. Indeed, correlations between early executive function measures and later IQ increased with age, while correlations with early *BSID* (Bayley, 1969) performance decreased with age. The visual recognition scores were also predictive of achievement at early school age (6 years). Children who were identified as having learning disabilities at this age (as indexed by a score >1SD below the mean on a standardised achievement test and an IQ score within 1 SD of the mean) were also more likely to have achieved poorer visual recognition scores as infants. In line with findings from non-clinical samples, these findings suggest that individual differences in early executive function may help to explain later achievement discrepancies in a large number of children born very preterm.

3.7 Limitations in Studies of Executive Function in Children Born Very Preterm

Despite increasing evidence for the role of executive function impairments in accounting for some of the achievement deficits in children born very preterm, there are a number of limitations with regard to these studies. Such limitations make it difficult to draw conclusions or establish consistency across results. Many of these limitations are similar to those for studies of general cognitive and academic outcomes in this population, which have been discussed above. As can be seen in Table 3.1, there is wide variation in the sampling frame of these studies and many fail to report recruitment rates, periods of recruitment and sample retention rates. Specifically, several studies have recruited children from single geographic areas, with little information provided regarding the regional or national representativeness of the samples (Korkman et al., 1996; Rose et al., 1989; Ross, Auld, Tesman, & Nass, 1992; Taylor et al., 2006). Some of these samples have been drawn from impoverished areas, where socioeconomic factors are likely to play a substantial role in the affecting the outcomes of children studied. With regard to study recruitment and retention rates, these have varied from as low as 30% of eligible participants, to above 90%. Clearly, poorly defined samples and low retention and recruitment rates severely constrain our interpretation of study findings.

Another general limitation of many of these studies is a failure to report descriptive statistics related to specific domains of executive function (Bohm et al., 2004; Esbjorn et al., 2006; Herrgard et al., 1993; Taylor et al., 2006). Not only does this make it difficult to examine the relative effect sizes across studies, it also precludes the description of areas of memory or attention that may present more difficulty for these children. There are specific difficulties in interpreting discrepant findings where studies have added task scores to form a composite measure of memory or attention performance.

A final issue with regard to this literature is that, where there are differences in executive function, effect sizes are generally small. However, effect sizes tend to be higher for studies with larger sample sizes, which suggests that some of these studies may have had limited power to detect group differences. Apart from this, the effect sizes for studies that have included the least mature infants appear to be higher (Anderson et al., 2004; Marlow et al., 2007; Taylor et al., 2006). In helping to explain the discrepant findings across these studies, there is the possibility that correlates of preterm birth, such as medical, neurological and socio-environmental experiences, may moderate or mediate the relationship between preterm birth and executive function. A consideration of the role of these factors is likely to be of value in helping to identify those children who may be most at risk of executive impairment.

Collectively, these studies suggest that executive function may be an area of difficulty for children born very preterm, with differences in executive function being found across different ages and on multiple measures. The most robust findings are in the area of spatial working memory, with effect sizes for these studies often being moderate to large. In contrast, few studies have reported deficits in verbal working memory. Studies assessing problem solving, strategising and planning have also generally found that children born preterm fare less well than their full term peers. This may be related to an impaired ability to generate a sequential strategy and analyse its success. While studies have generally reported behavioural differences in attentional regulation in children born very preterm, it is unclear whether these children have specific difficulties in sustained attention, inhibitory control or in the ability to shift attentional set. Further research into the specific domains of executive control that may be affected in children born very preterm will be important in helping to clarify these issues. The examination of these aspects of executive function in a large, unselected cohort, with attention to a range of socio-familial and medical correlates of very preterm birth is also likely to help overcome some of the previous limitations in this literature.

Table 3.1: Summary of Studies of Executive Function in Children Born Very Preterm and/or Very Low Birth Weight

Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Rose et al. (1989).	<1500g (760-1450g)	Hospital sample, The Bronx	46	45	7 mo	1979-1981	82%	Novelty preference for patterns and faces *	Information processing, memory, attention	0.46	Prospective design with novel measures. Showed positive associations between these early measures and later performance on measures of memory and cognition, helping to establish the importance of early measures of information processing for later cognitive development.
Ross et al. (1992).	28-32 weeks (M bw =1462.9g)	Hospital sample, New York	30	30 with grade I/II IVH 30 with no IVH	10 mo C	NR	NA	Novelty preference task*†† A-not-B task	Information processing, attention, memory Spatial working memory	0.25, 0.65 NS	Conducted discriminant function analysis to identify tasks that best differentiated groups, which has ‘real world’ benefits in terms of discriminant validity. Measures correctly classified 67% of children into subgroups. Examined associations between SES, ethnicity and outcomes. Several children in the very preterm group could not pass initial ‘training’ trials of A-not-B, making it difficult to ascribe their difficulties to working memory as opposed to learning or memory per se.

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Hergard et al. (1993).	<33 weeks GA	University Hospital, Finland	60	60	5 yrs	1984-1986	98%	NEPSY attention test	Attention Memory	NS	Groups matched for gender and SES. Non-parametric tests used where applicable. Results including and excluding children with severe neurodevelopmental delay presented. Only composite scores reported.
Frisk and White (1994).	<30 weeks, <1000g	Hospital, Ontario	68 (27 no PVL/ IVH, 26 Grade I or II IVH/ PVL, 15 Grade III IVH/ PVL)	20	6 yrs	1984-1987	NR	Peabody Picture Vocabulary Test† Expressive Vocabulary Test† Verbal Fluency Test Token Test†† Digit Span Test†† Self-Ordered Pointing † Verbal Learning Test††	Receptive vocabulary Expressive language Fluency/ abstraction Sequencing Verbal working memory Working memory Long term recall and recognition memory	NC	Performance levels decreased with increasing severity of neurological injury. Performance of groups of children born preterm without injury and children born full term was comparable. As items on the complex receptive language measure grew more complex, children in the groups with neurological lesions showed lower scores, highlighting the advantages of examining performance scores in detail.

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Katz et al. (1996).	<34 weeks (26-34)	Hospital sample, London	64 divided by severity of IVH/ PVL (ultra sound)	40	6-8 yrs	1983-1985	30%	Continuous Performance Test -errors of omission* -errors of commission*	Sustained attention Inhibitory control	0.62 0.52	Groups matched for age, gender and ethnicity. Mean age of full term group 1 month higher than preterm group. Very preterm and full term samples were similar in terms of SES. CPT task probably placed high requirements on working memory. Children with most the severe neural abnormalities were unavoidably excluded because they could not complete the task.
Korkman etal. (1996).	<1500g M=1178	Hospital sample, University of Helsinki	43 <1500g 34 <1500g & SGA (>2SDs below M for GA)	45	5-9 yrs	NR	NR	NEPSY knock & tap/keep eyes closed tests NEPSY sustained attention* Digit span Word span	Inhibitory control Sustained attention Verbal working memory	NS	Separated out children born SGA and VLBW. Examined associations between outcomes and other medical risk factors, e.g. RDS, IVH & length of oxygen requirement. The group of children born AGA were of lower mean gestation and birthweight than those born SGA, making comparisons difficult.

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Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Matthews et al. (1996).	<2500g (1633-2475)	Letters sent out from birth records, Minnesota	10	10	7 – 15 mo C	NR	NA	A-not-B A-not-B looking Barrier detour task Means-end task	Working memory/ inhibitory control Working memory Inhibitory control Problem solving	NS	Longitudinal performance examined (28-60 weeks). Small sample size. 100% recruitment. Looking and reaching paradigms used so that the two manipulations could be compared. A description of the medical profile of the preterm group is not provided.
Rose and Feldman (1996).	<1500g, <37 weeks	Hospital sample, The Bronx	50	40	11 yrs C	1979-1981	83%	Visual recognition memory* Cognitive Abilities Test & Specific Cognitive Abilities Test* WISC-R*	Attention, memory, information processing Memory & processing speed General cognitive ability	0.64 0.34-0.69 0.81	Low SES sample; 44% SGA. Assessed memory errors and reaction time independently, which helps to control for motor impairments. Assessed effect of very preterm birth in relation to level of difficulty of tasks, with increasing cognitive load interacting with birth status. Memory and processing speed accounted for group differences in IQ.

Table 3.1: Summary of Studies of Executive Function in Children Born Very Preterm and/or Very Low Birth Weight

Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Ross, Boatright, Auld,and Nass (1996).	<27 weeks	Hospital sample, New York Control group matched for SES, gender and race	27 with grade 1 or 2 IVH 28 with no IVH	27	2 yrs	NR	94%	Novelty preference Invisible displacement task* Object discrimination reversal*	Information processing, memory, attention Object working memory Strategic search Flexibilty/set-shifting	NS 0.85 0.66 1.16	Group of children with no IVH was matched for birthweight, days of ventilation, gender, ethnicity and SES index. No information provided regarding recruitment rates. Children with moderate to severe neurosensory deficits or substance exposure in utero excluded. No children showed cysts on ultrasound. Novelty preference task used – difficulty determining what this is measuring Good use of different versions of the task with variations in difficulty/cognitive demands.
Wilcox et al. (1999).	<37 weeks (32-35) <2500g (1800-2570)	Three metropolitan hospitals, USA	21	18	2.5 to 6.5 mo C	NR	NR	Expected/ Unexpected event	Working memory for object location Attention	NS	Controlled for confounding factors by conducting a second control study. Most participants from middle class households. Recruitment rates not reported

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Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Mellier and Fessard (1998).	<33 weeks M=29.3	NA	12	56	12 yrs	1985-1986	NA	Tower of Hanoi* Stroop colour-word task*	Planning/problem-solving Inhibitory control	NC	Small sample size. Comparison with a sample of adolescents with frontal lobe lesions means more robust assessment of "frontal system deficit hypothesis." Observed the strategies/ reasons for failure of children as they performed the TOH task. No information about medical factors, social background factors or extent of frontal lobe lesions in the group with frontal lobe damage provided. Results are described only, with no scores presented.
Pasman et al. (1998).	<34weeks (25-34)	Hospital sample, Nijmegen, Holland	44 with low medical risk.	18	5 yrs	1983-1984	73%	Visual search task* Auditory discrimination test	Selective attention Auditory sustained attention	NC	Examined the overlap between low cognitive/neurological scores and found that the group differences were largely attributable to a small group of severely impaired children, showing importance of analysis of individual factors relating to development.

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Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Harveyet al. (1999).	<1000g (743-949)	Hospital sample, Queensland	30	50	4-5 yrs	1990-1991	63%	Tower of Hanoi* Finger sequencing task* Tapping test*	Planning/problem -solving Motor fluency Inhibitory control	NC	Two tests relied heavily on fluent motor responses. Poor sample retention. Some consideration given to medical factors (e.g. related younger gestational age and days of ventilation to performance). High rates of ROP (50%) in sample.
Luciana et al. (1999).	<40 weeks (24-39)	Hospital sample, selected Controls matched for age	40	92	7-9 yrs	1987-1989	NA	CANTAB* Psychomotor screening CANTAB spatial memory span* CANTAB working memory task* CANTAB Tower of London* CANTAB intradimensional/ extradimensional set-shift	Speed and accuracy of fine motor response Working memory Working memory Planning/problem -solving Set-shifting	0.45 0.56 0.82 0.36 NS	Low recruitment rate (62%) possibly indicates non-representative sample. Very heterogeneous sample with wide range of medical risk. CANTAB tests largely independent of motor speed/accuracy Tasks allow for comparison between groups at various levels of difficulty

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De Haan et al. (2000).	<37 GA (27.3-37.1)	Neonatal follow-up clinics	16 born 35-37 weeks GA 16 born 27-34 weeks GA	16	19 mo C	NA	NA	Immediate and delayed elicited memory for -actions -sequences*	Explicit memory	0.94	Low risk sample, (no grade III/IV IVH, no SGA, minimal ventilation) Showed a linear effect of GA group on outcome. Detail in design highlighted specific facets of memory that may be a challenge for children born very preterm.
Isaacs et al. (2000).	<1500g, <30weeks GA	Selected from larger study	11	8	13 yrs	1982-1985	NA	Rivermead Behavioural Memory Test* Wechsler Memory Scale* Logical memory Children's Auditory Verbal Learning Test* Design learning* Rey-Osterieth Figure	Everyday memory (e.g. messages, stories, faces) Memory for stories and designs Prose recall Verbal memory and learning Pattern learning and memory Memory	NC	Forward digit span similar between the two groups; backwards was different. Differences on the test of everyday memory evident for delayed or prospective memory. Differences in other tests were predominantly in learning. Few other differences when specific tests were examined. Highly selected sample. The level of detail in operationalisation of one construct (memory) is good.

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Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Rushe et al. (2000).	<33 weeks	Hospital sample, London	75	53	14-15 yrs	1979-1980	83%	Trails B test Digit span FAS verbal fluency*	Set-shifting/flexibility Verbal working memory Fluency/ abstraction	NS NS 0.73	Older cohort may not be representative of medical experiences today. Voluntary control group. Examined digit span as one score rather than looking at short term/working memory components Replaced 8% of data with group mean. Gender & SES covaried in between-group analyses.
Bohm et al. (2002).	<1500g 23-36 weeks GA	Regional sample, Stockholm Controls identified from birth register	182	125	5.5 yrs	1988-1993	87%	NEPSY selective attention* NEPSY verbal fluency test* NEPSY sorting test NEPSY colour-form test* NEPSY impulse control test*	Selective attention Fluency/ abstraction Set-shifting/ flexibility Set-shifting/ flexibility Inhibitory control	0.27 0.42 NS 0.53 0.33	Control group recruitment rate very low (42%). Although a large group were SGA, this was controlled for in data analysis The relationship between medical risk and EF was not examined. Groups did not differ in terms of maternal/paternal education.

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Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Curtiset al. (2002).	<40 weeks (24-40)	Hospital sample, selected	32	25	9-14 yrs	1987-1989	78%	CANTAB motor screening CANTAB spatial memory span* CANTAB spatial working memory* CANTAB Tower of London CANTAB intradimensional /extradimensional set-shift	Speed, accuracy Spatial working memory Spatial working memory Planning/ strategising Set-shifting	NS 0.31 0.75 NS NS	Only 78% of sample born preterm – mixed NICU sample. Examined results in relation to a medicate risk composite. Shows graduated nature of impairments, whereby those in the NICU group showed more deficits on the more difficult tests.
Espy et al. (2002).	<37 weeks (28-36.5) 739-2475g	Regional intensive care unit, Illinois Control group matched for maternal education, sex and age	29	29	2-3 yrs	NR	NA	Delayed alternation* Spatial reversal	Spatial working memory Set-shifting /flexibility	0.75 NS	Sample restricted to children with no IVH>2, CLD, PVL or BPD. Tasks adapted from established animal paradigms, therefore allowing some indication of possible neurological substrates. An analysis of the types of errors made was useful.

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Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Landry et al. (2002).	M bw = 1111g, M GA=29.7	NS	163	90	3, 4 & 6 yrs	1990-1992	86%	Independent play Spatial reversal task	Goal-directed strategising Set-shifting/flexibility	NS	Looked at specific parenting behaviours in relation to executive function in children born preterm. Measures did not distinguish between the two groups, so it is not possible to ascertain how parenting behaviours relate to performance discrepancies in this group. Sample was of low SES, posing difficulties for generalisability of results.
Elgen et al. (2004).	<2000g	Regional, Hordaland (Norway)	130	170	11 yrs	1986-1988	75%	CPT –Errors of omission* (before adjustment family confounding factors and IQ). -Errors of commission Stroop colour-word test	Sustained attention Inhibitory control Inhibitory control	0.35 NS NS	Assessed specific aspects of attention. Excluded children with CP or neurosensory impairment. Low sample retention. Looked for potential confounding factors, such as visual acuity, motor tempo, hearing and medication first. Statistically controlled for socio-familial factors, such as differences in parental nurturance, parental education and smoking during pregnancy. Used a parental rating measure of attention (CBCL) to cross-validate.

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Anderson et al. (2004).	<28weeks /<1000g (M=884)	Regional, Victoria Full term group recruited randomly from birth records.	275	265	8-9yrs C	1991-1992	89%	Tower of London* Digit span* Rey Complex Figure* Behaviour Rating Inventory of Executive Function	Planning/problem solving Verbal working memory Strategy/planning Parent reported executive behaviour	0.21 0.35 0.64 0.31	High recruitment (92%) Randomly selected control group from same hospital matched for age, race and health insurance. Looked at reverse as well as forward digit span so separated short term vs. working memory SES was covaried in analyses. Significant results remained when children with significant neurosensory impairment were excluded

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Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Bohm et al. (2004).	<1500g, <37 weeks	Regional, Stockholm	182	125	5.5 yrs C	1988-1993	85%	NEPSY impulse control* NEPSY token test* NEPSY selective attention* NEPSY verbal fluency* NEPSY colour/form test* Digit span Word span Knox cube test* Behaviour rating*	Inhibitory control Working memory Selective attention Fluency/ abstraction Set-shifting/flexibility Verbal working memory Spatial working memory Distractibility Activity Mental effort	NC	Used corrected age for very preterm group. <37 weeks and <1500g suggests many may have been SGA. Used non-parametric tests where applicable. Covaried for IQ. Examined influence of medical factors (CLD, ROP, IVH, PVL).

Table 3.1: Summary of Studies of Executive Function in Children Born Very Preterm and/or Very Low Birth Weight

Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Vicari et al. (2004).	<34 weeks (29-34) <2330g (910-2330)	Children involved in paediatric follow-up, Rome.	19	19	3-4 yrs	1998		Visual search* Spatial working memory test*	Selective attention Memory for location Recall over different delays	0.9 0.84-1.29	Full term control group matched for age, SES and IQ. Low gestation combined with higher birthweight range suggests many children may have been SGA. Low risk cohort (IQ>90, no abnormalities on ultrasound). Various degrees of difficulty/delay on spatial memory task assessed Difficult to determine representativeness of sample, as children were recruited from follow-up clinics.

Table 3.1: Summary of Studies of Executive Function in Children Born Very Preterm and/or Very Low Birth Weight

Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Taylor et al. (2004).	<1500g	Regional sample, Ohio	48 <750g 47 750-1500g	52	Mean 16.8 yrs	1982-1986	73%	CANTAB spatial memory span**	Spatial working memory	1.93	Good description of sample drop-outs, who were lower in SES and cognitive scores. Groups matched for birth, age, ethnicity and gender and similar in SES – these were included as covariates in analyses. Examined outcomes in terms of means and cut-off scores (1 standard error below expected scores). Repeated analyses excluding children with neurosensory impairment or IQ<70 and covarying for vocabulary scores. These analyses showed differences in verbal and language measures were attenuated so that they were no longer significant. Examined outcomes in relation to a variety of medical and neurological factors. Children born <750g distinguished from those born <1500g in analyses.
								CANTAB intradimensional/ extredimensional shift	Set-shifting/flexibility	NS	
								CANTAB stockings of Cambridge**	Planning/problem-solving	0.60	
								CANTAB spatial working memory **	Spatial working memory	1.1	
								CANTAB rapid visual processing**	Verbal working memory/vigilance	0.78	
								Contingency Naming Test**	Fluency/set-shifting	1.2	
								Rey Complex Figure**	Strategy/planning	0.88	
								Word fluency test**	Verbal fluency	0.64	

Table 3.1: Summary of Studies of Executive Function in Children Born Very Preterm and/or Very Low Birth Weight

Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Caravale et al. (2002).	<34 weeks (30-34) <2500g (910-2400)	Children enrolled in paediatric follow-up.	30	30	3-4 yrs	1998	65%	Visual search* Spatial location memory test*	Selective attention Memory for location	1.08 1.1	No children had abnormalities on ultrasound. Full term control group matched for age, gender and SES. Children born very preterm recruited from follow-up clinics. Sample of older gestational age. Covaried results for IQ
Mikkola et al. (2005).	<1500g <27weeks	National cohort, Finland	206	NA	5yrs	1996-1997	NR	NEPSY attention/EF composite*	Attention Executive function	0.46	Composite measures prevent meaningful analysis of specific areas of difficulty
Woodwardet al. (2005).	<33weeks GA, M=27.9 <1500g M=1088	Regional neonatal intensive care unit, Canterbury	100	103	2yrs C	1998-2000	93%	Multi-step-multi-location task*	Working memory for location	0.28-0.38	Showed that pattern of errors on this task was developmentally atypical in children born very preterm, highlighting importance of consideration of executive function within a developmental framework. Considered clinical and neurological factors, with significant relationships shown between performance and maternal fever/sepsis at delivery, white matter abnormalities and cerebral spinal fluid volume.

Table 3.1: Summary of Studies of Executive Function in Children Born Very Preterm and/or Very Low Birth Weight

Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Bayless and Stevenson (2006).	<32 weeks (23-32) 460-2210g	Hospital records (30% recruitment) No IVH >2	40	41	6-13 yrs	NR	NA	TEA-Ch 'sky search' TEA-Ch 'score' TEACH-Ch 'creature counting'* TEACH-Ch 'walk'* CANTAB working memory	Selective attention Sustained auditory attention Set-shifting Inhibitory control Spatial working memory	NS NS 0.92 0.53 NS	Voluntary control group used (letters sent home from school) so possibly non-representative. No between-group differences in mean postcode classification of SES. Tasks were analysed with and without adjustment for IQ. Univariate and multivariate analyses were performed.
Esbjorn et al. (2006).	<1000g/ <28 weeks	National cohort - Denmark	207	76	5 yrs C	1994-1995	91%	NEPSY immediate and delayed recall (29 children in preterm group) NEPSY keep eyes closed, knock and tap and avoid pointing (EF composite created)	Memory Executive function	NS NS	Groups were matched for corrected age, gender, parental education. Memory tests were for short term and long term memory for names and faces, but not working memory. All executive function tests reliant on motor control. Attrition rate for NEPSY was very high and only children with higher IQ scores participated. A full IQ test was completed, which allowed for subtest comparisons.

Table 3.1: Summary of Studies of Executive Function in Children Born Very Preterm and/or Very Low Birth Weight

Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Kulseng et al. (2006).	<1500g M=1178	Population based, Norway	54	83 (& 60 SGA)	14 yrs	1986-1988	NP	Knox cube test* CPT-2 – Errors of omission Errors of commission Stroop* Trail-making test* Wisconsin Card Sort*	Spatial working memory Sustained attention Inhibitory control Inhibitory control Set-shifting /flexibility Set-shifting working memory/ inhibitory control	0.51 NS NS 0.40 0.66 0.64	Little information regarding medical risk profile of participants. Used non-parametric tests where appropriate. Analysed groups with and without cerebral palsy. Generated cut-off scores to compare 'poor performance' estimates across groups as opposed to looking at means only.
Taylor et al. (2006).	<1000g	Hospital cohort, Cleveland	219	176	Mean 8 yrs	1992-1995	92	NEPSY tower, design copying, arrows, visual search, comprehension of instructions, list learning scores used to form composite EF and memory score.*	Planning/problem solving, memory, selective attention.	0.73	Full term group matched for class, school, DOB & gender. High mortality rate (25%). SES co varied in analyses. Examined outcome in relation to a wide range of medical factors. Composite combined many different cognitive skills, making it difficult to isolate specific areas of impairment. Repeated tests excluding multiple births and children with cognitive score <70.

Table 3.1: Summary of Studies of Executive Function in Children Born Very Preterm and/or Very Low Birth Weight

Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Martel, Lucia, Nigg, and Breslau (2007).	<2500g	Random selection from 2 hospital databases, (city and suburb)	473 (25 <1000g, 132 SGA)	350	6 yrs	1983-1985	75%	Child Behaviour Checklist* Diagnostic Interview Schedule * Continuous Performance Task -Beta -D-prime -Reaction time -Commission errors -Omission errors	Inattention/ hyperactivity Symptoms of ADHD Activation/ inhibition Arousal Response speed Inhibitory control Sustained/ selective attention	0.34 0.30 NS	Conducted mediation and moderation analyses and found partial mediation of the effect of low birth weight on attention by motor control and arousal on the CPT. Also tested for a moderating effect of gender. Combined multiple sources of measurement. Correlation between low birth weight and arousal was very small (r=0.09).
Sansaviniet al. (2007).	25-33 weeks 550-1630g	NR	62	28	3.5 yrs C	1997-1999	NR	Test of non-word repetition* Word span	Phonological short term/working memory Phonological short term/ working memory	0.47-0.69	30% of children born preterm vs. 7% born full term could not complete the non-word repetition test. Authors showed an association between working memory skills and grammatical competence, with those children who could not complete the non-word repetition task showing the poorest scores on measures of grammar.

Table 3.1: Summary of Studies of Executive Function in Children Born Very Preterm and/or Very Low Birth Weight

Study	**Gestational age / birthweight group**	**Sample pool**	**N preterm**	**N control**	**Age**	**Year of birth**	**Sample retention**	**Measures**	**Constructs assessed**	**Effect size (*d*)**	**Comments, Strengths & Limitations**
Marlow et al. (2007).	<26 weeks	National, UK	180	158 class mates	6 yrs	1995	78%	NEPSY Tower* NEPSY statue/knock-tap* NEPSY visual attention (visual search)*	Planning, monitoring Inhibitory control Selective attention	NC	Children with CP excluded from analysis. Male gender was shown to be significantly associated with lower executive function performance.
Nosarti et al. (2007).	<33 weeks	College hospital, London	61	64	20-25	1979-1982	33%	Sentence Completion Test* Controlled Oral Word Association* Trail Making Test Test of Attentional Performance*	Initiation, inhibition and planning Verbal fluency Shifting Divided attention Inhibitory control Attentional lapses	0.6 0.53-0.87 NS NS NS 0.57	Low sample, retention with higher IQ in those retained. Voluntary control group could indicate self selection bias. Group born very preterm took longer on Trail Making Test, but did not make more errors. Earlier study of cohort showed no executive difficulties, highlighting importance of longitudinal follow up. All differences persisted when IQ, gender and age were statistically controlled. No relationships between measures of perinatal risk and executive function.

Table 3.1: Summary of Studies of Executive Function in Children Born Very Preterm and/or Very Low Birth Weight

Study	Gestational age / birthweight group	Sample pool	N preterm	N control	Age	Year of birth	Sample retention	Measures	Constructs assessed	Effect size (*d*)	Comments, Strengths & Limitations
Edgin et al. (2008)	<33 weeks, <1500g	Regional, Canterbury	92	103	2-4 yrs C	1998-2000	93%	Multi-step-multi-location task (2 yrs)* Detour reaching Box (4 yrs)**	Working memory for location Inhibitory control/ set-shifting	0.28-0.38 0.18-1.49	Longitudinal analysis showed continuity in executive function performance from age 2 to age 4 years. Examined relationships with MRI data from term (See Table 4.1). Large effect sizes (*d*=1.13/1.49) for differences between preterm children with severe neurological abnormalities and children born full term, moderate differences for children with mild abnormality vs. children born full term (d=0.49-0.81) and small effects for differences between preterm children with no abnormality vs. full term children (d=0.03-0.18).

* Comparison of preterm group to full term control group showed significant differences in favour of full term group (p<0.05); **Comparison of ELBW with full term group showed significant differences in favour of the full term group; † Comparison of preterm group with severe neurological lesions showed significant difference in favour of full term group (p<0.05); ††Comparison of preterm groups with mild and severe neurological lesions showed significant difference in favour of full term group and preterm group without lesions (p<0.05); NR: Not reported; NA: Not applicable for study; NS: No significant difference; NC: Not able to be calculated C: Corrected for prematurity; Yrs: Years

Chapter 4

Potential Mediating and Moderating Mechanisms in the Association between Very Preterm Birth and Executive Function

It is important to consider the developmental mechanisms that may account for potential executive function impairments in children born very preterm. Identifying the factors and processes that lead to executive impairments is challenging because preterm birth forms part of a matrix of medical, neurological and socio-environmental influences, all of which may be associated with cognitive development. Consequently, some researchers have designated children born very preterm a “double hazard” population (Nadeau, Boivin, Tessier, Lefebrvre, & Robaey, 2003, p. 235). Biological and social risks may both contribute to preterm delivery itself and continue to act in an additive or transactional way. Three broad sets of factors are correlated with very preterm birth and may be important in the development of executive impairments. These include medical or clinical risk factors, neurological factors and socio-environmental factors. A review of these factors is provided below.

4.1 Associations between Clinical Factors and Executive Function

Studies of global cognition in children born very preterm have been consistent in showing a greater risk of cognitive impairment with decreasing GA and birthweight (Koller, Lawson, Rose, Wallace., & McCarton, 1997; Laptook, O'Shae, Shankaran, Bhaskar, & NICDH Neonatal Network, 2005; Vohr et al., 2000). Studies of executive function appear to replicate this trend. For example, when comparing children born ELBW (<750g) and children born VLBW (750-1500g) to a group of full term class peers at age 16 years, Taylor et al. (2004) found that children born

ELBW scored significantly lower than the full term group on several neuropsychological measures. These included CANTAB measures of spatial working memory, planning and vigilance (Fray et al., 1996), the Rey Complex Figure (Bernstein & Waber, 1996) and the Contingency Naming Test (Anderson, Anderson, Northam, & Taylor, 2000), a measure of set-shifting. In contrast, there were no significant differences between the performance of children born VLBW and full term, although visual inspection of the reported mean scores indicated a linear pattern, whereby the VLBW group achieved scores slightly lower than children in the full term group. This suggests a gradient effect, whereby lower birthweight may be associated with greater executive function difficulties.

There has been less evidence for a within-group effect of continuous measures of gestation and birthweight when only children born very preterm are considered (Anderson et al., 2004; Curtis et al., 2002; Rose & Feldman, 1996). For example, Rose and Feldman (1996) reported no correlation between birthweight or gestational age and scores on various measures of spatial working memory within a group of 11 year old children born VLBW. Similarly, although Anderson et al. (2004) found that there were some significant differences in the executive function performance of children born extremely preterm (<750g/<26 weeks GA) compared with those born at higher gestational ages (26-27 weeks GA, 750-1000g), there were only weak correlations between gestational age and these outcome measures (r=.001-0.19). One possible explanation for these findings may be the large variation in medical experiences for children born very preterm. When they are considered as a group, it may be that gestation or birthweight acts as a good proxy for later impairments but further understanding of individual differences warrants a closer inspection of the impact of various individual clinical experiences within this group of children.

One factor that may be an important moderator of the effect of very preterm birth on later executive function is gender. Male gender is associated with a greater risk of very preterm birth, as well as higher mortality and morbidity (Elsmen, Pupp, & Hellstrom-Westas, 2004; Ingemarsson, 2003; Pollack & Birnbacher, 2004). Several studies have documented poorer cognitive and neurodevelopmental outcomes in males born very preterm when compared with their female counterparts (Laptook et al., 2005; Marlow, 2004; Whitaker et al., 1997). In studies that have examined gender in relation to attention and executive function, there has also been some indication that males are at more risk than females from an early age (Elgen et al., 2004; Marlow et al., 2007; Martel, Lucia, Nigg, & Breslau, 2007; McGrath et al., 2005). Thus, there is a possibility that male gender interacts with the level of prematurity or medical risk that children are exposed to, but these findings are in need of further investigation.

Added to this, several medical factors, including intrauterine growth restriction (IUGR), intrauterine infection, chronic lung disease (CLD) and respiratory distress, early (<72 hours after birth) or late onset (> 72 hours after birth) sepsis, patent ductus arteriosis (PDA), retinopathy of prematurity (ROP) and necrotising entercolitis (NEC) are associated with very preterm birth and rates of these medical morbidities are known to increase with decreasing gestation (Hack & Fanaroff, 2000). Definitions of these medical complications are provided in Appendix A. Most of the extant literature relating to very preterm birth and cognitive outcome has considered groups of children born very preterm as homogeneous, with little regard to the different medical experiences that these children and families experience. In studies that have given some consideration to this issue, a common practice is to examine outcome in relation to medical risk indices, which consist of a composite of children’s exposures to neonatal complications (Girouard et al., 1998; Landry, Denson, & Swank, 1997; Laucht, Esser, & Schmidt, 1997). For example, Luciana et al. (1999) used a composite risk score, summing infection, the degree of ventilation and neurological risk factors (IVH and PVL). This score was predictive of later spatial working memory (*r*=.36), spatial memory (*r*=-0.52), and strategy use in problem solving (*r*=0.36) in a group of children who had been in the NICU after birth. These findings suggest that level of overall illness may be a good marker for later difficulties in executive function.

However, a major limitation of this approach is that it does provide any information as to the specific factors that may make some children more vulnerable to later executive function difficulties. The most that can be concluded is that the sickest, most medically fragile infants are at greatest risk for later difficulties and that the effect of these risk factors is potentially additive. There is a need for the identification of important constituent factors if findings are to assist in the provision of targeted intervention or the development of specific treatments for these children.

Studies that have examined the influence of specific medical risk factors have shown that very preterm children who experience CLD are more likely to achieve lower scores on standardised cognitive and achievement tests than those who do not (Hack & Fanaroff, 2000; Laucht et al., 1997; McGrath & Sullivan, 2002; Taylor et al., 2004; Vohr et al., 2000). Furthermore, continuous measures of the days that children spend on oxygen or ventilatory support have been shown to predict term neurobehavioural scores (Brown, Doyle, Bear, & Inder, 2006), as well as scores on complex executive function and visuo-spatial measures during childhood (Rose & Feldman, 2000) and adolescence (Taylor et al., 2004). Apart from this, further studies have revealed correlations between NEC, length of stay in hospital (Taylor et al., 2006), ROP (Bohm et al., 2004) and measures of executive function, suggesting that the influence of these clinical complications warrants further exploration.

In response to these medical complications, the modern era of neonatal intensive care has introduced a number of medical advancements; the increased use of antenatal steroids and surfactant therapy has had major repercussions in terms of survival and morbidity (Hack & Fanaroff, 2000; Meadow, Bell, & Unstein, 2003). Less is known about the long term consequences of these medical interventions for cognitive development. Studies to date show that the administration of a single course of antenatal steroids is not associated with impairments in attention and working memory in either children or adults (Dalziel et al., 2005; LeFlore, Salhab, Broyles, Engle, & 2002). Indeed, there is some evidence that antenatal steroids may be associated with better self-regulatory competence in infancy and early childhood (Brown et al., 2006; Clark, Woodward, Horwood, & Moor, In press). However, postnatal steroids may be associated with poorer neurodevelopmental outcomes. Follow-up studies have shown that infants who have received postnatal steroids achieve lower scores on standardised neuropsychological and executive function (NEPSY) measures later in childhood (Laptook et al., 2005; LeFlore et al., 2002; Taylor et al., 2006; Vohr et al., 2000). It is important to note the difficulty in separating the effects of these drugs from the medical risk factors they are designed to treat. Nonetheless, continued investigation into the later developmental outcomes of children treated with them will help to inform medical practice and intervention.

This brief review of literature relating to clinical factors that may increase the vulnerability of children born very preterm to impairments in executive function has highlighted several factors worthy of further evaluation. These include gender, the extent of immaturity and/or growth restriction, the use of ventilation and prolonged oxygen dependence, the infant's exposure to infection as well as medical treatments administered to these infants. This study will therefore consider a range of clinical risk factors in relation to executive performance.

4.2 Associations between Neurological Factors and Executive Function

One difficulty in studying the clinical correlates of very preterm birth is that the mechanisms by which these factors exert their influence remain unclear. It is likely that at least some of the associations between these clinical risk factors and later executive function impairments are mediated by neurological alterations in children affected. Specifically, hypoxia and ischemia; respiratory distress; inflammation and infection; poor nutrition; and early exposure to a stressful extrauterine environment may have negative repercussions at a critical time for brain development (Perlman, 2001). Understanding of the neurological development in children born very preterm has previously been curtailed by the use of ultrasound imaging, which has poor resolution in comparison to newer imaging protocols (Childs et al., 2001; O' Shae, Counsell, Bartels, & Damman, 2005; Volpe, 1999). However, more recent MRI studies have rapidly increased understanding of the impact of very preterm birth on early neurological development.

Very preterm birth is associated with altered neurological development. White matter is especially vulnerable to injury or abnormality in children born very preterm (Miller et al., 2002). Two potential explanations for this have predominated in the literature. First, the cerebral vasculature of the preterm infant is immature. The area around the lateral ventricles, and the germinal matrix in particular, is extremely vulnerable to haemorrhage because capillaries in this region are primitive and therefore susceptible to rupture in response to blood pressure variations (Squier, 2002; Vergara & Bigsby, 2004; Volpe, 2001b). Additionally, it has been suggested that poorly developed arteries within the periventricular regions act as vascular end zones, or “watershed areas” (Volpe, 1999, p. 526). Infants who are medically unstable will experience frequent changes in cerebral blood flow, making these white matter areas of the brain vulnerable to ischemia (Volpe, 1999). From about 32 weeks

GA, blood vessels lengthen, mature and branch throughout the white matter, thus decreasing the vulnerability of infants of older gestational age (Perlman, 1998; Silveira & Procianoy, 2005).

Another possible reason for the vulnerability of white matter is that the time during gestation when very preterm infants are born is an important period for the division and growth of oligodendrocytes, the precursor cells for oligodendoglia. Oligodendrocytes are extremely fragile cells, prone to necrosis when free radicals and cytokines (stress hormones) are released after hypoxia-ischemia or infection (Dammann, Drescher, & Veelken, 2003; Silveira & Procianoy, 2005; Vohr & Ment, 1996). The germinal matrix acts as the precursor region for oligodendroglia and astrocytes, making this area particularly vulnerable (Volpe, 2001b).

The most common neural pathologies associated with very preterm birth include intraventricular haemorrhage (IVH) and perviventricular leukomalacia (PVL). Traditional ultrasound imaging, administered as part of routine neonatal care, is able to detect the majority of cases of IVH and more severe, cystic forms of PVL (O' Shae et al., 2005). IVH is haemorrhage into the germinal matrix tissue (Vohr & Ment, 1996). Haemorrhage is rated in severity from grade 1 (mild) to 4 (severe). Grades 1 and 2 are generally isolated to the germinal matrix or ventricles and do not cause ventricular dilation. Grades 3 and 4 are associated with bleeding into the parenchymal zone and ventricular dilation (Ross et al., 1992; Vohr & Ment, 1996). IVH generally leads to destruction of the germinal matrix and is associated with necrosis of the white matter surrounding the lateral ventricles and hydrocephalus (Vohr & Ment, 1996; Volpe, 2001b). Due to advances in medical intervention, the prevalence of IVH has declined (Darlow, Cust, Donoghue, & Australian and New Zealand Neonatal Network, 2003; Heuchan, Evans, Henderson, & Simpson, 2002), although rates were still approximately 15-20% in infants born <2000g in the 1990s

(Volpe, 2001b).

As well as IVH, ultrasound imaging is able to detect severe, focal forms of PVL, which manifest as cystic changes around the lateral ventricles of the brain, generally near the foramen of Monroe (Perlman, 1998). This severe form of PVL was first identified in 1962, after scientists observed the white spots (leukos) and softening (malacia) that appear on ultrasound images of the brain (de Vries, Groenendaal, & Meiners, 2002). Reports of the prevalence of severe PVL range from fewer than 3% to 26% of children born below 1500g, with cerebral palsy being the most commonly recognised associated outcome (Perlman, 1998; Rees & Harding, 2004; Silveira & Procianoy, 2005).

With recent developments in neuroimaging technology, it has become clear that PVL represents a spectrum of white matter abnormality, with a less severe, diffuse pattern of abnormality, which extends into multiple areas of deep periventricular white matter, being more common amongst children born very preterm (Back & Rivkees, 2004; Inder, Wells, Mogridge, Spencer, & Volpe, 2003; Perlman, 1998; Volpe, 2003). Table 4.1 provides an overview of findings from previous MRI studies of children born very preterm. As is clear from this table, these studies have varied in the types of imaging performed, the areas of the brain on which they have concentrated, the age groups they have studied and according to whether they have incorporated findings from developmental testing. One common limitation of these MRI studies is that they often involve small, select samples, with data loss due to poor scan quality being a common issue.

Nonetheless, it is evident from this table that studies have been consistent in identifying disturbances in the structural integrity of white matter areas of the brain (Abernethy, Cooke, & Foulder-Hughes, 2004; Cooke & Abernethy, 1999; Counsell, Rutherford, Cowan, & Edwards, 2003; Huppi et al., 2001; Huppi et al., 1996; Inder, Warfield, Wang, Huppi, & Volpe, 2005; Inder et al., 2003; Kesler et al., 2004; Nagy et al., 2003). Qualitative rating systems reveal thinning of the corpus callosum, increased ventricular size and diffuse high signal intensity on structural MRI scans (Inder et al., 2003; Maalouf et al., 1999; Olsen, 1998; Stewart et al., 1999), while volumetric studies show decreased white matter volumes over the whole brain, coupled with enlarged ventricles and thinning of the corpus callosum and other key white matter tracts (Abernethy et al., 2004; Boardman et al., 2006; Gimenez, Junque, Narberhaus, Botet et al., 2006; Inder et al., 2005; Kesler et al., 2004; Peterson et al., 2003).

Similarly, diffusion tensor imaging studies generally show higher levels of water diffusion in the brains of children born very preterm, suggesting altered or immature development of neural tracts (Boardman et al., 2006; Huppi et al., 2001; Miller et al., 2002; Nagy et al., 2003; Skranes et al., 2007). Indeed, one diffusion tensor study that employed serial imaging from birth to hospital discharge showed that apparent diffusion coefficients decreased with age in children with no or mild white matter abnormalities on structural MRI. In contrast, apparent diffusion coefficients did not change in infants with severe white matter abnormalities (Miller et al., 2002). This suggests that early white matter injury or abnormality may alter the long-term microstructural development of neural tracts. Given that white matter development has been shown to correlate with processing speed and cognitive performance in non-clinical samples (Mabbott, Noseworthy, Bouffer, Laughlin, & Rockel, 2006; Schmithorst, Wilke, Dardzinski, & Holland, 2005), early white matter abnormalities may have long-term consequences for cognitive development.

Coupled with cerebral white matter changes, studies have generally shown decreased total cortical volume, as well as decreases in the tissue volumes of subcortical nuclei in children born very preterm (Allin et al., 2001; Boardman et al., 2006; Inder et al., 2005; Kesler et al., 2004; Norsati et al., 2002; Peterson et al., 2003). Qualitative ratings and quantitative measurements at term equivalent age show reduced gyration and cortical folding, as well as reduced surface area of the brains of children born very preterm (Ajayi-Obe, Saeed, Cowan, Rutherford, & Edwards, 2000; Inder et al., 2005). This occurs in a dose-dependent manner with decreasing gestational age (Kappellou et al., 2006). In older children, quantitative studies have reported reductions in overall grey matter volume (Kesler et al., 2004; Norsati et al., 2002; Peterson et al., 2003) cerebellar volume (Allin et al., 2001; Peterson et al., 2000), hippocampal volume (Abernethy, Palaniappan, & Cooke, 2002; Isaacs et al., 2000; Norsati et al., 2002; Peterson et al., 2000) and caudate and thalamic volumes (Abernethy et al., 2004; Boardman et al., 2006; Gimenez, Junque, Narberhaus, Botet et al., 2006; Nosarti, Allin, Frangou, Rifkin, & Murray, 2005). However, others have reported that frontal and parietal volumes are enlarged relative to the whole brain in children born very preterm (Kesler et al., 2004; Peterson et al., 2003).

Some studies have reported associations between MRI measures and poorer performance on global IQ tests in groups of children born very preterm (Abernethy et al., 2004; Abernethy et al., 2002; Allin et al., 2001; Isaacs et al., 2004; Nagy et al., 2003; Olsen, 1998; Peterson et al., 2003; Peterson et al., 2000). However, far less is known about the relationship with specific cognitive outcomes. The gradual and progressive development of executive function across childhood, along with specific links between executive function tasks and neural networks, means that the study of such relationships could offer much promise both in informing our knowledge of brain-behaviour relationships and in determining specific aspects of neural development that may lead to poorer outcomes in these children.

In support of the relevance of neurological abnormalities for individual differences in executive function, previous research has shown a relationship between neurological abnormality identified by ultrasound and later executive function performance deficits in children born very preterm (Frisk & Whyte, 1994; Ross et al., 1992; Ross, Boatright, Auld, & Nass, 1996; Sherlock, Anderson, & Doyle, 2005). For example, two studies by Ross et al. (1992; 1996) demonstrated significant associations between less severe forms of IVH (grade 1 and 2) and children's performance on tests of attention/information processing, spatial working memory and set-shifting. In the first study, groups of children born very preterm (28-33 weeks GA) and full term were developmentally assessed at age 10 months. Children who had experienced grade 1 or 2 IVH were less likely to habituate when assessed with a novelty preference task. This possibly indicates that they did not process the stimuli as effectively as their peers or that they were less attentive. Children with IVH also performed less well on an A not B spatial location task than either children born preterm with no IVH or children born full term. Although children with IVH showed the lowest performance, there was a linear trend in scores, whereby children in the very preterm group without IVH also performed more poorly than those in the full term group. This suggests an effect of preterm birth independent of IVH.

In a second study at age 2 years, preterm children who had experienced grade 1 and 2 IVH showed poorer working memory and set-shifting performance than children without IVH and children born full term (Ross, Boatright et al., 1996). Children who had experienced IVH scored less well than those without IVH on an A not B type task. However, both preterm groups showed difficulties in conducting an organised search on this task, relative to children born full term. Children with IVH were also less likely to switch flexibly between responses on an Object

Discrimination Reversal set-shifting task (Deaehler & Butatko, 1974). Of interest, the preterm group without IVH did not demonstrate deficits on this set-shifting task, potentially helping to explain the previously reviewed discrepancies in findings related to set-shifting in children born very preterm. Another interesting findings was that the three groups in this study did not differ significantly in terms of their developmental scores on the *BSID* (Bayley, 1969), indicating that executive impairments may be independent of global cognitive or motor development.

It seems plausible that children with abnormalities detected by ultrasound imaging represent those at greatest risk for executive function impairments. However, the variability in performance of children without IVH in these studies suggests that abnormalities detected by ultrasound scanning may not sufficiently account for some of the more subtle executive function impairments seen in children born very preterm. Additionally, these studies are limited in terms of informing us about the effects of PVL because so few children meet criteria for PVL with ultrasound scanning. Therefore, more sensitive MRI measures of neural structure may help to better clarify the relationships between neural development and executive function.

As yet, however, few studies have examined executive function performance in relation to MRI, although a small number of studies have shown relationships between attention difficulties, rated on checklist measures, and MRI abnormalities (Abernethy et al., 2002; Nosarti et al., 2005; Skranes et al., 2007). Studies that have incorporated executive function measures have generally been completed with adolescents, have administered measures contemporaneously with MRI imaging and have reported discrepant findings (Allin et al., 2001; Gimenez, Junque, Narberhaus, Botet et al., 2006; Rushe et al., 2001). It is possible that differences in findings are related to different methods of MRI analysis (i.e. qualitative ratings vs. quantitative tissue segmentation) used in these studies. However, the discrepancies in findings also raise questions as the specific neural markers that may be associated with later executive performance and the capacity for compensation or recovery in children who show neurological abnormalities.

Only two studies to date have examined longitudinal relationships between term-administered MRI and early executive function in children born very preterm. Both of these studies have been conducted with the current New Zealand based cohort. The first study (Woodward, 2005), conducted with these children at age 2 years, showed that children born very preterm required more trials than children born full term to learn a retrieval strategy for a complex A-not-B search task involving multiple steps and obstacles (Zelazo et al., 1998). Children born preterm were also less likely to learn this search strategy after several trials. The preterm children who passed learning phases of the task showed a more random search strategy than their peers, suggesting that they had difficulty retaining a representation of the reward location in working memory. Analysis of the relationships between qualitative white matter abnormalities on MRI at term age and later task performance showed that, with increasing severity of white matter abnormality, children born very preterm were less likely to successfully complete this task. Successful performance was also correlated with higher proportions of cerebral tissue in the dorsolateral prefrontal, parieto-occipital, premotor and sensorimotor areas.

The second study (Edgin et al., 2008) demonstrated similar relationships between the extent of cerebral white matter abnormality at term and executive function performance on a measure of inhibitory control and set shifting (The Detour Reaching Box; Hughes & Russell, 1993) administered at age 4 years. Children rated as having mild and moderate-severe white matter abnormalities on MRI at term showed more evidence of perseverative behaviour during initial training phases of this task and less ability to flexibly switch between rule-based strategies when required. In contrast, children who showed no evidence of white abnormality at term age showed comparable performance to their full term peers. These studies suggest that early neurological abnormalities detected by MRI imaging may have prognostic value in identifying children at risk for later executive function impairments.

In summary, numerous studies have shown that children born very preterm are susceptible to abnormalities in neurological structure. While existing studies have sometimes demonstrated associations between these neural abnormalities and broad cognitive outcomes, studies have proven inconclusive as to what markers are particularly relevant. Furthermore, very few studies have prospectively examined the impact of early MRI measures of neurological integrity on later cognitive outcomes. Longitudinal studies may potentially provide information as to the predictive validity of these early neurological measures and provide a more comprehensive analysis of individual life-course processes that may mediate, moderate or contribute to longer-term outcome. Therefore, the current study will examine relationships between early MRI measures of cerebral white and grey matter abnormality and later executive function in a large cohort at early school age

Table 4.1: MRI Studies of Children and Adolescents born Very Preterm and/or Very Low Birth Weight

Reference	Sample	Measures	Key findings
Structural MRI studies of infants at term/ term equivalent age			
Huppi et al. (1999).	18 infants born preterm (28-32 weeks GA) with no severe medical complications, IVH or ischemia. 13 full-term infants.	Qualitative developmental staging system.	Less grey matter differentiation, gyration, cortical folding, white matter density and myelination in the preterm group.
Inder et al. (1999).	10 infants born very preterm (<32 weeks GA) with PVL. 10 without PVL. 14 full term infants.	Qualitative ratings of PVL from MRI scans in first 16 days. Quantitative tissue segmentation at term equivalent age.	Children with early PVL showed reduced cerebral grey matter volume (reduced by 28%) and myelination (reduced by 47%) at term and higher cerebral spinal fluid volume. Subcortical volumes were not significantly different. Qualitative ratings also indicated reduced gyral development in infants with PVL.
Maalouf et al. (1999).	41 infants born preterm (<30 weeks GA) scanned successively from birth to 38 weeks GA. 3 full-term infants.	Qualitative ratings of white matter appearance.	Incidences of ventricular dilation (most commonly in the anterior horns) increased in the preterm group from 37% at birth to 54% at term age. 12% of the preterm infants experienced lesions of the basal ganglia.
Ajayi-Obe et al. (2000).	14 children born extremely preterm (<30 weeks GA) serially scanned from birth. 8 full term.	Quantitative measures of cortical convolution and surface area.	Neural tissue volumes of children in preterm group did not differ from children born full term, but cortical folding and surface area were significantly reduced relative to children born full term.
Huppi et al. (2001).	20 infants born preterm (<32 weeks GA). 10 with white matter injury matched for GA to 10 with no white matter injury.	Diffusion-weighted MRI. ADC and relative anisotropy calculated and mapped for key white matter regions.	Infants with white matter injury showed disrupted orientation and density of fibres around the lateral ventricles, especially at the internal capsule.

Table 4.1: MRI Studies of Children and Adolescents born Very Preterm and/or Very Low Birth Weight

Reference	**Sample**	**Measures**	**Key findings**
Miller et al. (2002).	11 children born preterm (<36 weeks GA) with no white matter abnormality, 7 with minimal abnormality and 5 with severe abnormality.	Diffusion tensor MRI at birth and discharge. ADC values in selected white and grey matter regions.	In all groups, ADC values in grey matter regions decreased over time. In children with no abnormality/mild abnormality, ADC values decreased with age in white matter areas. In those with mild abnormality, ADC did not decrease in posterior areas and increased in frontal regions. In those with severe abnormality, ADC values in white matter areas did not change over time.
Inder et al. (2003).	100 infants born preterm (<33 weeks GA / <1500g).	Qualitative ratings of white and grey matter abnormalities.	20% showed moderate to severe white matter injury, with reductions in white matter. Only 29% were rated as showing normal white matter development. 27% showed grey matter abnormalities such as delayed gyral development and large amounts of extra cerebral space. Lower GA, sepsis, PDA, IVH and administration of ionotrophic steroids predicted white matter injury.
Counsell et al. (2003).	50 infants born preterm (25-34 weeks/500-2100g)	Diffusion weighted MRI ADC values in selected white matter regions.	Higher ADC values in infants with white matter lesions and high signal intensities suggested less development of white matter in these infants. ADC values were especially high in the frontal area.
Inder et al. (2005).	119 infants born preterm (<32 weeks GA/<1500g) 21 full-term controls.	Volumetric tissue segmentation and qualitative ratings of abnormality.	Preterm infants showed grey matter reductions of 20% and white matter reductions of 35%.
Boardman et al. (2006).	62 children born very preterm (<34 weeks GA). 12 full term	Volumetric analysis. Diffusion weighted MRI ADC values for key white matter areas, thalamus and lentiform nucleus.	Children in the very preterm group showed increased ventricular volume and reduced thalamic and lentiform nuclei volumes. ADC values were higher in the white matter regions of the very preterm group. Children born very preterm with high ADC values in the white matter showed reduced grey matter nuclei.

Table 4.1: MRI Studies of Children and Adolescents born Very Preterm and/or Very Low Birth Weight

Reference	Sample	Measures	Key findings
Structural MRI at term/term-equivalent age and outcome at follow-up			
Peterson et al. (2003).	10 children born preterm 14 children born full-term	Volumetric tissue segmentation. BSID at 2 years.	Parietal occipital grey matter volume was reduced in the preterm group, after covarying gender and head circumference. Grey matter volumes were enlarged in the dorsal prefrontal, orbitofrontal, premotor, subgenual and midtemporal regions in the preterm group. Volumes of the midbody, occipital and lateral areas of the ventricles were enlarged in the preterm group. White and grey matter volumes in the left sensorimotor and midtemporal cortices ($p<0.01$) were significantly correlated mental scale scores at 18 months (spearman's rho=0.72-0.95).
Woodward (2005); Woodward, Anderson, Austin, Howard, and Inder (2006).	92 children born very preterm (<33 weeks GA/<1500g) 103 children born full term	Qualitative ratings of white matter injury Volumetric tissue segmentation BSID and Object working memory task at age 2 years (see Table 3.1).	There were linear associations between extent of white matter abnormality, volume of cerebral spinal fluid and decreasing task performance. Cerebral tissue proportions in the dorsolateral PFC, premotor regions, sensorimotor regions and parieto-occipital regions were positively related to task performance.
Edgin et al. (2008).	88 children born very preterm (<33 weeks GA) 98 children born full term	Qualitative ratings of white matter injury Object working memory at 2 years Detour Reaching Box Task at 4 years (see Table 3.1).	There were linear associations between the extent of white matter abnormality on MRI and performance on the Detour Reaching Box Task. Children with mild to severe abnormality required a higher number of trials to learn rules of the task. Children with white matter abnormality made more perseverative errors on the final, set-shifting trials of the task, while children born very preterm with no white matter abnormalities performed comparably to peers. Children with white matter abnormalities were more likely to show consistent failure of executive function tasks across 2 and 4 years of age.

Table 4.1: MRI Studies of Children and Adolescents born Very Preterm and/or Very Low Birth Weight

Reference	Sample	Measures	Key findings
Structural MRI and developmental assessment during childhood			
Olsen (1998).	41 children born preterm (<1750) at 8 yrs 24 children born full term, matched for age, gender, twin status, maternal, SES and birth order.	Qualitative ratings of white and grey matter abnormality. Ventricular/brain ratio. WISC-R and NEPSY subtests administered.	Increased ventricular/brain ratio at the ventricular trigones was associated with lower scores on the block design test of the WISC-R (r = -0.4) and lower visual-motor integration scores on the NEPSY (r = -0.4). Volumes of the corpus callosum, frontal horn ventricular/brain ratio and midbody ventricular/brain ratio did not correlate with IQ. Children with PVL did not perform worse than other children born preterm on the IQ test.
Peterson et al. (2000).	25 children born preterm (<1250g) at 8 yrs. 39 term born children at 7-9 yrs. WISC-3 administered at 8 yrs.	Volumetric tissue segmentation from structural MRI.	Volumes of the cortex, cerebellum, basal ganglia, amygdala, hippocampus and corpus callosum were significantly smaller in the group of children born preterm. Ventricles were larger in the group of children born preterm. Differences in volumes of regions excluding the orbitofrontal, dorsal prefrontal and inferior occipital regions remained significant after covarying total brain volume and height and when children with IVH were excluded from analysis. Correlations between IQ subtests and brain volumes ranged from 0.2-0.63.
Nagy et al. (2003).	9 children born preterm (<1500g) with high distractibility scores on the NEPSY at 10-11 yrs. Children with IQ<80, IVH or PVL excluded. 10 children born full-term matched for gender and age.	Diffusion tensor MRI FA mapping.	Mean FA levels were lower in the in the corpus callosum and internal capsules of the preterm group. Brain sizes in the preterm group were decreased. 3 of the preterm children were found to have white matter reductions that were not diagnosed by ultrasound.
Abernethy et al. (2004).	105 7-8 yr old children born preterm (<32 weeks GA).	Volumetric measures of hippocampus and caudate nuclei. WISC-III IQ.	19% showed lesions on MRI, including PVL, ventricular dilation, thinning of the corpus callosum and porencephaly. When children with lesions on MRI were excluded, total brain volume correlated with performance IQ (r=0.25). There were significant correlations between IQ and caudate volumes (r= 0.28-0.37). There were no significant correlations between IQ and hippocampal volumes.

Table 4.1: MRI Studies of Children and Adolescents born Very Preterm and/or Very Low Birth Weight

Reference	Sample	Measures	Key findings
Kesler et al. (2004).	73 children born VLBW (<1250g) at 7-11 yrs. 33 children born full term.	Volumetric tissue segmentation. WISC-III IQ, Reading and math achievement tests.	Mean volumes of cerebral grey and white matter were reduced in the preterm group. Grey matter in the temporal lobes was significantly reduced in the preterm group; grey matter volumes in the frontal and parietal lobes were increased. Subcortical grey matter volumes were reduced in the preterm group. Increased birthweight was correlated with decreased parietal grey ($r = -0.32$), frontal grey ($r = -0.23$) and occipital horn ($r = -0.23$) volumes. Reduced subcortical grey matter was associated with IVH ($r = -0.27$). No neurological measures were correlated with cognitive outcome.
<u>Structural MRI in adolescence</u>			
Gimenez, Junque, Narberhaus, Bargallo et al. (2006).	50 adolescents born very preterm (<33 weeks GA) at 12-18 years (PVI excluded) 50 born full term matched for age, handedness, SES.	Volumetric tissue segmentation.	Children born very preterm did not show grey matter reductions or increased cerebral spinal fluid. Children born very preterm showed reduced density of white matter across several areas of the brain (frontal, occipital and temporal lobes, cingulate, corpus callosum, right optic radiation complex, superior, inferior and occipital faliculus).
<u>Structural MRI and developmental assessment in adolescence</u>			
Stewart et al. (1999).	72 adolescents born preterm (<33 weeks GA) at 14-15 yrs. 22 children born at term	Qualitative ratings of white matter abnormality. Reading and spelling tests, behavioural checklist, neurological exam.	55% of the preterm group showed abnormalities on MRI, including ventricular dilation, thinning of the corpus callosum, cysts or abnormal white matter signal. Less than 1% of full term children showed such abnormalities. More children in the preterm group showed abnormal neurological scores and lower reading ages, but this did not correspond with abnormalities on MRI scans. MRI abnormalities corresponded with more greater behavioural impairment levels.
Isaacs et al. (2000)	11 adolescents born VLBW (<1500g/<30 weeks GA) at median age 13 yrs 8 term-born controls	Qualitative ratings of white matter abnormality. Neuropsychological battery of memory tests (see Table 3.1)	Mean left and right hippocampal volumes were lower in children born preterm. Mean hippocampal volumes explained a significant amount of variance in scores on the everyday memory test ($r^2 = 0.45$).

Table 4.1: MRI Studies of Children and Adolescents born Very Preterm and/or Very Low Birth Weight

Reference	Sample	Measures	Key findings
Allin et al. (2001).	67 adolescents born preterm (<33 weeks) at 14-15 yrs 47 age-matched term-born controls	Volumetric tissue segmentation of cerebellum based on grid scoring system. IQ, Trail making, Digit Span, reading, spelling, Rey figure and verbal fluency.	Mean volumes of the cerebellum were significantly smaller in the group born preterm after covarying SES, gender and whole brain volume. Mean whole-brain grey matter volumes were lower in the group born preterm but differences in white matter volumes were not significant. There were significant relationships between cerebellar volume and full scale WISC scores (•=0.24), block design (• = 0.27), object assembly (• = 0.26) , K-ABC (• = 0.33), reading age (• = 0.30) and digit span scores (• = 0.25) in children born preterm.
Rushe et al. (2001).	As in Stewart et al. (1999) 75 adolescents born preterm (<33 weeks) at 14-15 yrs. 53 term-born controls.	Battery of neuropsychological measures (see table 3.1).	There were no differences in neuropsychological performance in those whose MRIs were rated as normal, equivocal or abnormal.
Abernethy et al. (2002).	87 adolescents born VLBW (<1500g) at 15-16 yrs. 8 term-born controls.	Volumetric measures of corpus callosum, caudate nuclei and hippocampus. IQ and behaviour scores from age 13 yrs.	Mean right and left caudate volumes and the ratio of left to right hippocampal volumes were reduced in the preterm group. Those with low IQ scores (<85) had significantly smaller right caudate volumes. Children classified as having attention deficits at 13 years had lower hippocampal volumes.
Nosarti et al. (2002).	68 adolescents born preterm (<33 weeks GA) at 14-15 yrs. 48 control adolescents born full-term	Volumetric grid-based measures of hippocampus, lateral ventricles, whole brain, grey matter and white matter.	Mean whole brain volumes, cortical grey matter volumes and hippocampal volumes were decreased in the group born preterm after covarying height and gender. Mean lateral ventricular volumes were higher in children born preterm. Children with PVL on ultrasound scans in infancy showed reduced white matter. Brain volumes did not differ significantly between groups classified as having no disabilities, moderate disabilities or severe disabilities according to a neurological exam.

Table 4.1: MRI Studies of Children and Adolescents born Very Preterm and/or Very Low Birth Weight

Reference	Sample	Measures	Key findings
Isaacs et al. (2004).	65 adolescents born preterm (<30 weeks) with no identified neurological disabilities at 12-16 yrs.	Voxel-based mapping of grey and white matter and hippocampal volume. WISC administered at 7 yrs & 16 years.	Approximately 50% of adolescents showed a decrease in IQ over time. Verbal IQ scores decreased by approximately 9 points on average and performance IQ by 12 points. Adolescents who showed a large decline in verbal IQ scores over time had significantly more white matter and less grey matter in the frontal region. Adolescents who showed a large drop in performance IQ had less grey matter in the hippocampal region and temporal lobe, but more white matter in the temporal lobe and parietal lobe.
Cooke and Abernethy (1999).	87 adolescents born VLBW (<1500g) at 15-16 yrs. 8 term-born controls.	Qualitative ratings of white matter abnormalities. Corpus callosum, caudate nucleus and brain size. IQ, achievement tests, behavioural checklist, psychiatric assessment.	42.5% of those born VLBW showed abnormalities on MRI scans, including ventricular dilation, thinning of the corpus callosum and porencephaly. 0% of controls showed such abnormalities. Mean corpus callosum and whole brain areas were lower in the group born preterm. Rates of ADHD and low IQ scores were similar in those with abnormalities on MRI and those without.
Nosarti et al. (2005).	72 adolescents born preterm (<33 weeks) at 14-15 yrs 50 term-born controls matched for age and gender.	Volumetric grid measures of caudate and whole brain volume. Behaviour checklist hyperactivity score.	Mean caudate volumes were reduced in the group of preterm adolescents - left caudate volume by 7% and right by 5% after covarying whole brain volume. Lower caudate volumes were significantly correlated with higher hyperactivity scores (r = -0.28 - -0.43).
Gimenez et al. (2006).	30 adolescents born very preterm (<33 weeks GA) at mean age 14 years. 30 full term matched for gender, handedness and SES.	Volumetric tissue segmentation of thalamus into grey and white matter and cerebral spinal fluid.	Participants in the group born preterm showed significantly less white matter and cerebrospinal fluid and lower intracranial volumes. All areas of the thalamus were volumetrically smaller in the group born preterm. Scores on verbal fluency tasks correlated significantly with thalamic volumes (r=0.56 – 0.72) in the group born preterm.

Table 4.1: MRI Studies of Children and Adolescents born Very Preterm and/or Very Low Birth Weight

Reference	**Sample**	**Measures**	**Key findings**
Skranes et al. (2007).	34 adolescents born VLBW (<1500g). 120 born full term. Age 15 years.	Diffusion tensor imaging with FA mapping. IQ and psychiatric symptoms.	VLBW group showed lower mean FA values in the internal capsule, external capsule, corpus callosum, superior fascicles, interior fascicles and external fascicles. In VLBW group, lower IQ correlated with lower FA values in the superior, interior and external fascicles. Inattention and ADHD symptoms correlated with lower FA in external, middle and inferior capsules.

Note. FA: Fractional anisotropy (measure of amount of diffusion); ADC: Apparent diffusion coefficient (measure of restriction of water); PFC: Prefrontal cortex.

4.3 Associations between Socio-Familial Factors and Executive Function

In addition to clinical and neurological factors, the socio-familial experiences of children born very preterm are likely to be important in the development of executive function. Consideration of such factors is likely to impact on our understanding of executive function in children born very preterm by two principle means. First, as mentioned above, it is known that children born very preterm are more likely to be born into environments that are financially and socially disadvantaged. Demographically, minority ethnicity, low SES, young maternal age and single marital status are associated with preterm birth (Martius et al., 1998). These may be considered ‘selection factors,’ in that children born very preterm are often naturally selected into a population with less social capital, more stress and lower social and financial resources. Consideration of these early socioeconomic discrepancies is important because these factors may act as confounding influences, potentially explaining or exacerbating the vulnerability of children born very preterm to poorer executive outcomes relative to their peers. Therefore, consideration of between-group differences in SES is important.

Second, the early socio-familial experiences of children born very preterm are important because these factors may mediate or moderate the effects of early medical compromise in these infants, either exacerbating the effects of children’s medical fragility or fostering resilience against poor medical and neurological odds (Laucht et al., 1997). A large corpus of animal literature supports the role of early stimulation and social participation in contributing to neural development and complexity (Sackett, Novak, & Kroeker, 1999). The study of these influences may help to identify children who are at increased developmental risk. Therefore, within-group variations in social experience are also of importance.

The first potentially influential socio-familial factor that shall be considered in this study is SES. A wealth of literature has clearly demonstrated that low SES or poverty is associated with poorer cognitive and academic achievement (NICHD Early Child Care Research Network, 2005; Pike, Iervolino, Eley, Price, & Plomin, 2006). Furthermore, studies have recently begun to suggest that executive function may be one specific neurocognitive domain where SES is likely to have a larger differential impact (Farah et al., 2006; Noble et al., 2007; Noble, Norman, & Farah, 2005). This may be because the protracted development of executive function allows more time for a multiplicity of environmental influences to have an effect.

Several studies demonstrate that measures of SES are correlated with the cognitive outcomes of children born very preterm (Dezoete & MacArthur, 2000; Ross et al., 1991; Siegel & Ryan, 1989; Taylor et al., 1995; Taylor, Klein, Schatschneider, & Hack, 1998; Thompson et al., 1997) and that SES may operate with medical risk in an additive manner (Bradley et al., 1994). In a New Zealand based study (Dezoete & MacArthur, 2000), children born VLBW (<1500g) whose parents were of professional or managerial employment status obtained higher scores on the *Stanford-Binet Intelligence Scales* (Thorndike, Hagen, & Sattler, 1986) at age 4 years than children whose parents were in manual labour or unskilled employment roles. A similar pattern of findings emerged for behavioural measures, with children in the higher SES groups being rated by examiners as less attentive and by parents as more hyperactive. Unfortunately, no control group was recruited for this study, so it is not possible to determine whether the effects of SES were additional to effects of prematurity.

Although most studies have employed only one measure of SES, lower SES is associated with several other family and social factors that may exert ongoing influence on children’s development (Farah et al., 2006; Pike et al., 2006). Research with non-clinical samples has identified several risk and protective factors that are associated with long term cognitive and academic achievement in children. Among these are single parenthood, family instability, level of stress in the household and maternal mental health (Laucht et al., 1997; Sameroff, Seifer, Baldwin, & Baldwin, 1993).

To investigate the impact of these familial risk factors, Gross, Mettelman, Dye, and Slagle (2001) assessed 118 preterm infants and 119 term infants at approximately 10 years of age as part of a longitudinal study. Social factors such as maternal marital status and maternal education at the time of birth were associated with school grade retention and special education in the preterm group and not in the full term group. Specifically, only 9% of children born very preterm whose parents were married were receiving special education, while 26% of those whose mothers were single were receiving special education. Additionally, children who had contact with both parents were less likely to require educational assistance. Preterm children who had no changes in caregivers and fewer moves to different houses were also less likely to require special educational assistance. This is of interest, given that parents of children born very preterm have a higher risk of divorce than those of children born full term (Swaminathan, Alexander, Boulet, & 2006).

Added to these social background factors, mothers of infants born very preterm report higher stress levels, both economic and psychological (Singer et al., 1999) and there is also an association between preterm birth and maternal depression (Davis, Edwards, Mohay, & Wollin, 2003; Shandor-Miles, Holditch-Davis, Schwartz, & Scher, 2007). The relationship between maternal depression and anxiety and cognitive outcomes in children in the general population has been well documented (Hay et al., 2001; Milgrom, Westley, & Gemmil, 2004; Petterson & Albers, 2001) and maternal depression has also been shown to be associated with poorer language and behavioural outcomes amongst children born very preterm (Miceli et al., 2000). Therefore, these factors may be also important for children's executive function development.

However, the above studies do not reflect the fact that more distal influences such as poverty and social risk may exert their effects through the parent-child relationship, perhaps because these environmental circumstances mean that parents are more stressed and less available to their children. Theory and research suggest that children learn gradually to regulate their own attention, behaviour and activity through mutual experiences with their primary caregiver (Feldman, Greenbaum, & Yirmiya, 1999; Kopp, 1982; Ruff & Rothbart, 1996; Schore, 1994). As well as this, parents can provide scaffolding for children's learning about concepts, rules, connections and problem-solving processes through their use of verbal explanations and guidance (Winders-Davis, 2003). Scaffolding that is timely and that shifts in accordance with the child's needs and abilities has been found to be most appropriate (Salonen, Lepola, & Vauras, 2007). Finally, the interactional synchrony of the parent-child relationship may be important in understanding developing executive competencies. Interactions where the behaviours of the parent and child are mutually reciprocal, bidirectional and follow on from in each other in a predictable, timely way, are likely to be most conducive to the children's regulation and learning (Feldman et al., 1999).

The importance of parental scaffolding for the development of executive function in children born preterm is illustrated in a recent Structural Equation Modeling analysis including children born preterm (<36 weeks GA) and full term (Landry et al., 2002). This research showed that higher levels of maternal verbal scaffolding and facilitation of problem-solving during a toy interaction task at age 3 years predicted stronger language skills in children at age 4 years. In turn, language skills at age 4 were related to children’s spatial working memory and goal-directed toy play at age 6 years. The model applied across both groups of children in the study. Findings suggest that early parent-child interactions contribute to important skills such as language, which in turn contribute to children’s ability to be strategic and goal-focused during independent problem solving.

Parents can, however, sometimes disrupt children’s focused attention and goal-directed behaviour by being too controlling of interactions or overwhelming in their stimulation (Ruff & Rothbart, 1996). For example, Assel, Landry, Swank, Smith, and Steelman (2003) found that maternal directiveness (the provision of structured information that did not allow children to choose options for themselves) during a 10-minute play interaction and during everyday activities at age 2 years was negatively associated with children’s executive behaviour during play at age 4. Again, this pattern of relationships was consistent across groups of children born preterm (<36 weeks) and full term. Therefore, levels of maternal sensitivity and intrusiveness are likely to be important facilitators of executive competence in children born very preterm.

Although they have been relatively neglected in the past, it is clear that social and familial factors play an ongoing role in the development of all children. Indeed, additive or interactive effects mean that these factors may be even more important for children who have biological vulnerabilities. Social background factors need to be considered both in relation to the documented discrepancies in achievement between children born very preterm and children born full term and in relation to the ongoing development of these children as individuals. Rather than examining each of these factors in isolation, comprehensive models of their interacting influence are required in order to understand the continuing dynamic between nature and nurture.

This chapter has examined four important mechanisms of influence that may contribute to executive function outcomes in children born very preterm. First, the variation in medical experiences and level of illness in these children may be important in the genesis of difficulties. Second, neurological factors such as brain injury or abnormality during the early neonatal period may disrupt myelination and neural development, potentially having ongoing effects on the development of higher cognitive processes. Third, the social environment within which the child is reared may be influential in terms of buffering against stress and access to stimulating learning experiences and nutrition and health services. Finally, the relationship that is established between the parent and child is likely to play a vital role in either compensating for or exacerbating the effects of early medical risk. Few researchers have examined these factors in sufficient depth to provide a comprehensive understanding of influential mechanisms behind executive function impairments in children born very preterm. The detailed complexity of individual experience demands complexity in the measures we use to quantify these experiences. The current study aimed to address this issue by examining individual differences in executive function outcomes of children born very preterm in relation to a broad range of medical, neurological and socio-familial indicators.

Aims and Hypotheses

Against this background, the research questions and aims of this thesis were as follows:

1) *Aim:* To describe the executive function profile of children born very preterm age 6 years. Specific domains of interest included: a) working memory, b) planning and problem solving, c) sustained and selective attention d) inhibitory control e) self-monitoring and f) set-shifting.

   Hypothesis: Children born very preterm group will show lower performance on laboratory, parent reported, teacher reported and observational measures of executive function. Executive function impairment will be pervasive across all domains tested. Specific areas of executive function hypothesised to be most impaired are spatial working memory and attention.

2 a) *Aim:* To examine associations between a range of medical risk factors and performance on measures of executive function within a group of children born very preterm.

   Hypothesis: Executive function performance scores will show a negative correlation with neonatal risk factors such as birth weight, gestational age, IUGR, maternal infection, sepsis and oxygen dependence within this group of children.

b) *Aim:* To determine the degree to which measures of executive function are related to cerebral white and grey matter abnormalities as rated from qualitative MRI imaging at term equivalent age in children born preterm.

Hypothesis: White matter and grey matter abnormalities, as assessed on the basis of qualitative ratings of MRI scans at term, will be associated with lower performance across executive function measures at age 6 years.

c) *Aim:* To examine associations between a range of social background and parenting experiences and performance on measures of executive function within children born very preterm.

Hypothesis: Measures of parenting, SES and family structure will correlate significantly with children's subsequent performance on executive tasks.

3) *Aim:* To determine the utility of measures of executive function in accounting for academic achievement difficulties in children born very preterm.

Hypothesis: Performance on measures of executive function in very premature children will predict value difficulties in academic achievement, independent of differences in general cognitive function

Chapter 5

Method

5.1 Design

This research was conducted as part of a prospective, longitudinal cohort study into the effects of being born very preterm and/or VLBW on children's later developmental outcomes (Inder et al., 2005; Woodward et al., 2006; Woodward, 2005). The sample for this larger study consists of a regionally representative cohort of 106 children born very preterm (<1500g; <34 weeks GA) and a comparison group of 113 full term control children (>36 weeks GA) matched for gender and time of birth. As part of this study, children have been assessed with a range of measures throughout the perinatal period, at term-equivalent (40 weeks) gestational age, 1, 2 and 4 years adjusted age. The current study focuses on children's outcomes at age 6 years. A broad overview of the wider study design is presented in Figure 5.1. A detailed description of the study sample and measures included in this thesis is provided below.

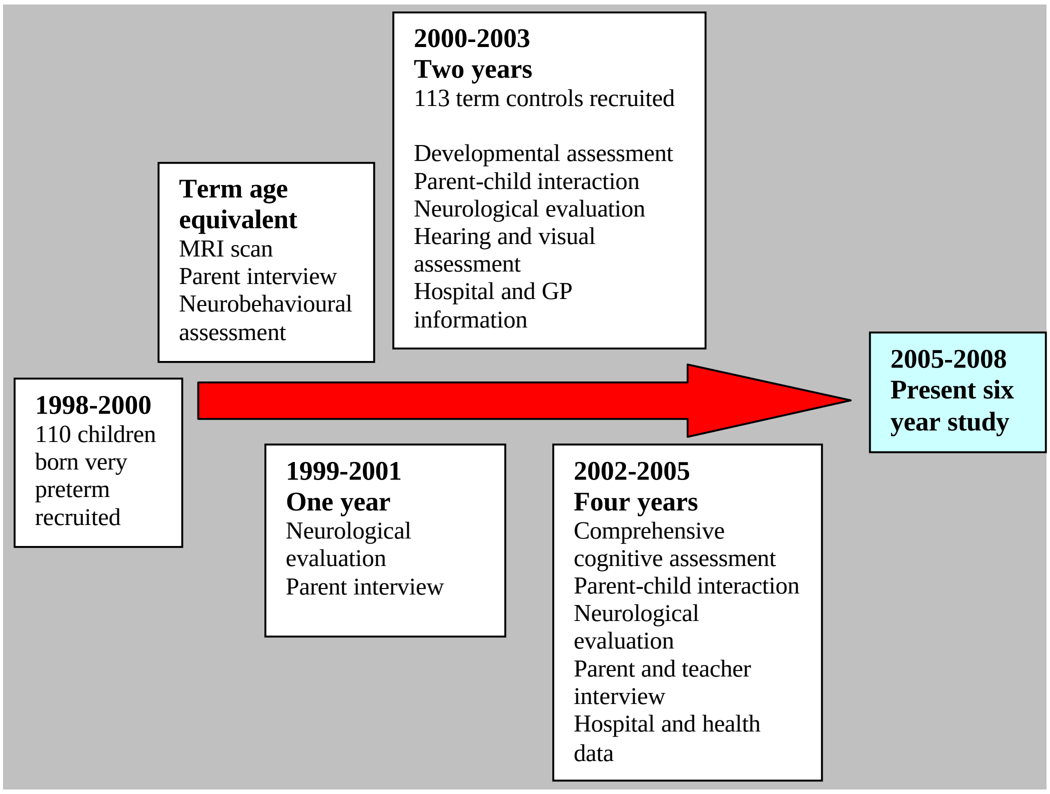


Figure 5.1: Overview of Longitudinal Study of Children Born Very Preterm and Full Term

5.2. Participants

The initial sample for the study included two groups of children. The original recruitment procedure for these groups of children is detailed below, followed by a description of the recruitment procedure for the current follow-up study.

5.2.1. Children Born Very Preterm

The first group of participants consisted of 106 children born very preterm and/or VLBW. These children were born at Christchurch Women's Hospital and consecutively admitted into a level III neonatal intensive care unit between July 1998 and November, 2000. This unit represents the sole provider for the greater Canterbury area.

Following the birth of their baby, parents were approached by one of the neonatologists on the unit or a research nurse and invited to participate in the study.

To be eligible for inclusion, infants were required to have been born below 33 weeks GA or to have weighed less than 1500g at birth. If, however, children were of multiple births and one child met these inclusion criteria, all surviving children were included in the study. Children with congenital abnormalities at the time of birth or whose parents did not speak English were excluded. A total of 129 infants born during this period were eligible for inclusion in the study. Of these, 10 died before term age, 4 failed to be recruited and 5 families refused to participate. Thus, excluding those who died, 92% of eligible participants were recruited, leaving 110 children born very preterm. A further three infants died within the first year of life. One child was also subsequently excluded because of a history of intellectual impairment in the family.

Amongst this original group of 106 children born very preterm, 51% were male and 34% were multiple (twin) births. Birth weights in this group ranged from 385g-1790g, with a mean of 1064.46 (313.09)g. Gestation ranged from 23-33 weeks, with a mean of 27.87 (2.35) weeks. The range of days spent in hospital was 37-184, with a mean length of stay of 78 days. Ten percent of these infants had intrauterine growth restriction (IUGR, defined as birthweight >2SDs below that expected for gestational age) and 34% still required oxygen at 36 weeks.

5.2.2 Term Control Children

When very preterm infants reached 2 years of age, a comparison group of 113 children born full term (37-41 weeks GA) and of normal birthweight (>2500g) was recruited. These children were identified by selecting a child born second previous or second next to each child in the preterm cohort from the hospital database. The parents of these children were traced and invited to participate in the study. Of the 180 full term children and families approached, 64% (n=116) agreed to participate. Three children were excluded because they failed to meet inclusion criteria. Of the

64 children who were not recruited, 47% were not traced, 12.5% refused participation, 12.5% had moved overseas and 28% agreed to participate, but were not seen within the pre-specified window for assessment due to illness, family death or repeated failure to attend the appointment. Between group comparisons of children and families who did or did not participate in the study showed that there were no significant differences in terms of mean birthweight ($p=0.18$), gestational age at birth ($p=0.14$), gender ($p=0.68$), family SES ($p=0.91$), minority ethnicity ($p=0.62$) or the proportion of single parents ($p=.56$). The only significant difference to emerge was for maternal age. Mothers who were unable to be contacted or recruited tended to be older ($p<0.001$). Of the remaining children, 55% were male and 3.5% were of multiple birth. The birthweights of these children ranged from 2690 to 4630g, with a mean of 3583.97g. Gestational ages for this group ranged from 37-41 weeks, with a mean of 39.53 weeks.

A comparison of SES data (collected at age 2 years) for the full term group with regional data for the greater Canterbury area (Statistics New Zealand, 2001) is shown in Figure 5.2. Categories of SES were based on the Elly Irving SES Index (Elly & Irving, 2003), an instrument derived from the 2001 New Zealand census data. SES brackets 1-2 represent professionals and managers, brackets 3-4 are semi-skilled professionals and tradespersons, while brackets 5-6 represent manual labourers and elementary professions. As can be seen from this figure, in comparison with data collected during the 2001 census, the breakdown of family SES in the full term group was comparable, suggesting that, in terms of their socioeconomic circumstances, the families in this group were representative of the larger region from which they were recruited.

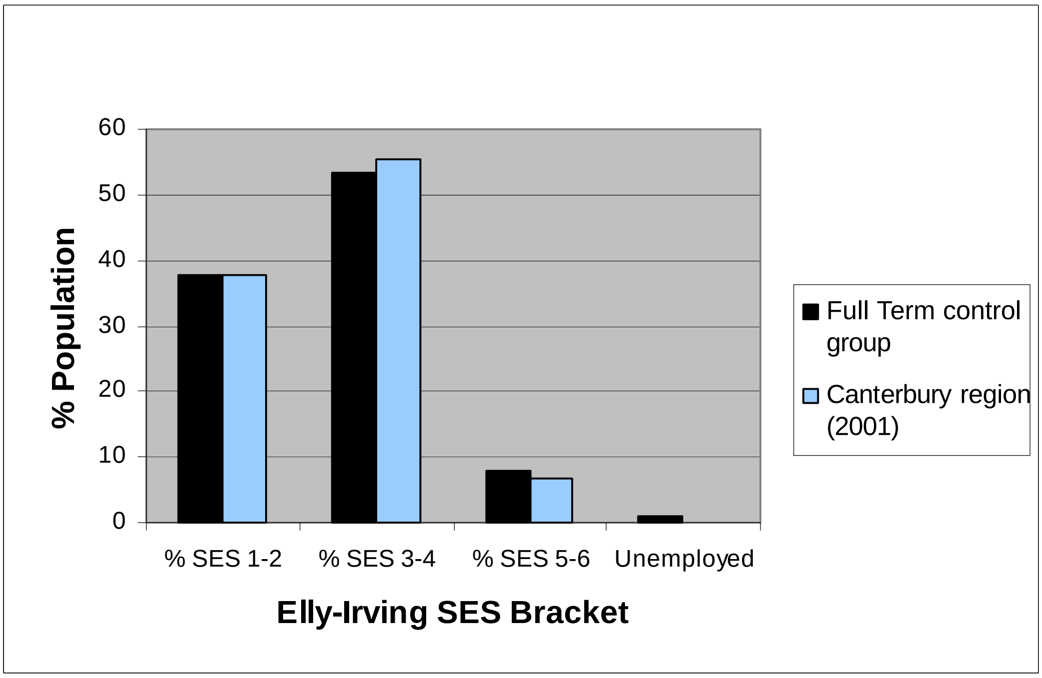


Figure 5.2: Comparison of Full Term Control Group Socioeconomic Status with Census Data for the Canterbury Region

5.2.3 Recruitment at Age 6 Years

Figure 5.3 shows sample retention rates from birth to age 6 years for groups of children born very preterm and full term. As shown, 103 children born very preterm and their families agreed to participate in the current 6-year follow up study. Three families of children born very preterm were not recruited because parents refused due to personal reasons or time involvement. This represented a sample retention rate of 97% for the very preterm group. One of these participants was blind. Although this child was seen at age 6 years, she was unable to complete many of the tasks. Thus, for the purposes of analysis, the sample size for the very preterm group generally consisted of 102 children.

With respect to the full term group, 108 of the 113 potential full term participants agreed to participate. Of those participants who were not seen, 4 were unable to be traced and one initially agreed to participate, but declined to schedule an appointment after several attempts. This represented a sample retention rate of 96% for the full term control group.

An analysis of available data comparing the 8 children who declined to participate or were untraced at age 6 to the remainder of the sample showed that those who did not participate did not differ significantly in terms of mean gestation ($p=0.7$), birthweight ($p=0.6$), gender ($p=0.86$), SES ($p=0.74$), ethnicity ($p=0.61$), maternal age ($p=0.1$) or maternal education ($p=0.19$).

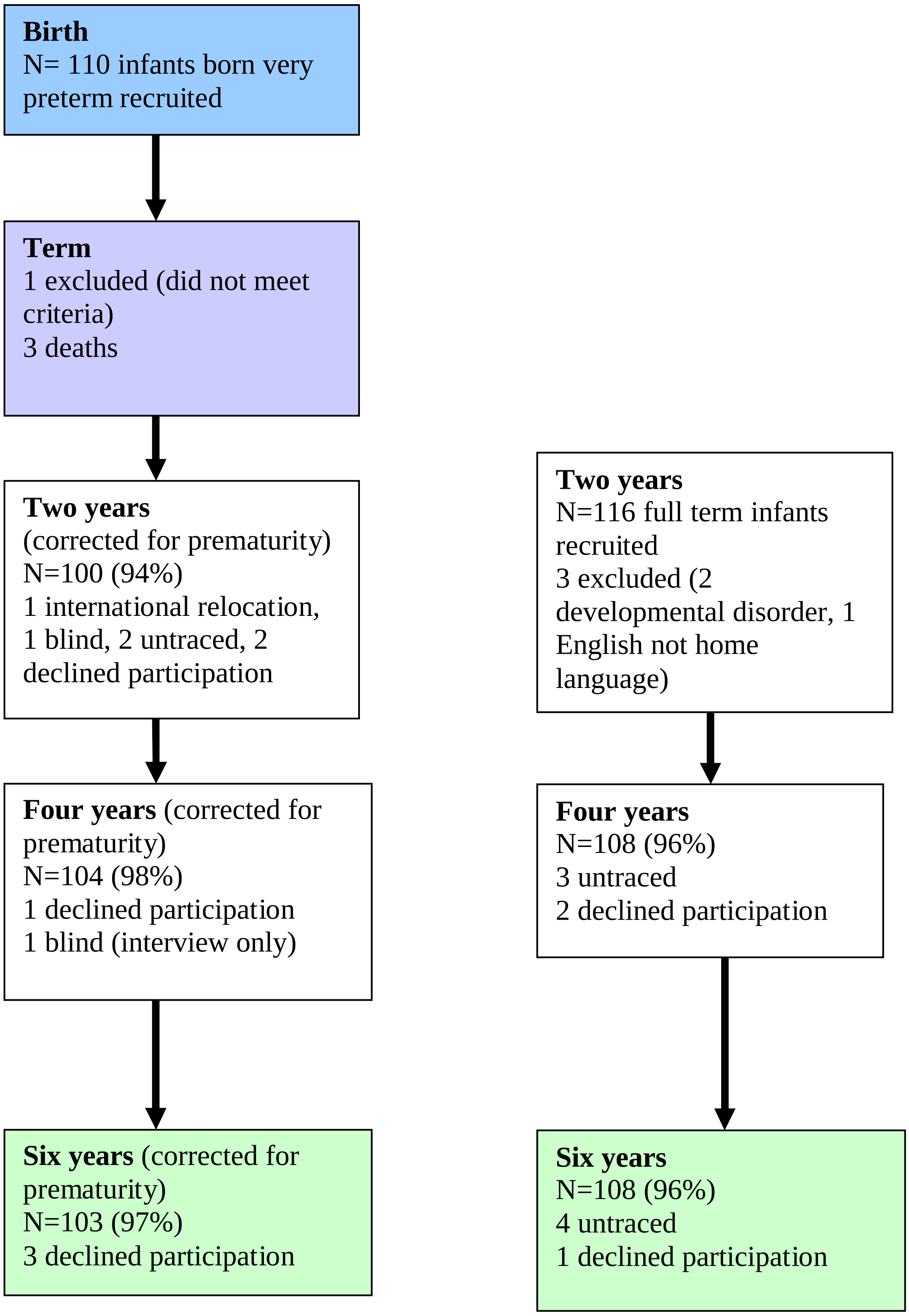


Figure 5.3: Flow Chart of Participation of Children Born Very Preterm and Full Term from Birth to Age 6 Years

5.2.4 Sample Characteristics

Table 5.1 shows the early clinical, social and neurodevelopmental characteristics of children born very preterm and full term. As expected, children in the very preterm group were smaller and lighter at birth than their full term counterparts ($p<0.001$). Additionally, there were more twins in this group ($p<0.001$) and they were more likely to have experienced IUGR ($p<0.01$). As groups had been matched for gender, there were no group differences in the ratio of males to females ($p=0.64$).

Within the very preterm group, there was considerable variability in medical experiences, with a large range in the number of days children stayed in hospital and the extent of ventilatory support children required. While there were few cases of proven maternal infection, approximately one third of mothers were administered antenatal antibiotics, suggesting that the suspected level of infection during pregnancy may have been higher. Furthermore, in most cases, antenatal steroids were administered, in keeping with current trends (Meadow et al., 2003). As can be seen from this table, levels of neurological injury (PVL and IVH), as diagnosed by bedside ultrasound, were low.

As well as being more medically compromised, children in the very preterm group were more likely to have experienced a number of adverse socio-familial factors than their full term peers by age 6 years. These families tended to be of lower SES, as shown by lower mean scores on the Elly-Irving SES scales and by the fact that more of these families had an income below $25 000 per annum at age 6 years ($p<0.01$). In terms of their family make-up, children born very preterm were as likely as those born full term to be born to single parents ($p=0.14$). They were no more likely than those born full term to be born to younger mothers ($p=0.45$). There was a tendency for children in this group to come from homes that were less stable, with an elevated rate of parental changes (as a result of divorce or separation, gaining or losing step-parents, experiencing the long term absence of a parent or being fostered or adopted) experienced in this group, relative to their full term peers (p=0.10). However, group differences did not reach statistical significance.

Finally, Table 5.1 also shows the neurodevelopmental characteristics of the sample. Analysis of the proportion of children with neurosensory and motor impairments in each group showed a greater tendency to be wearing glasses by 6 years of age (p=0.06). However, only one child in the very preterm group met criteria for legal blindness. Four children in the very preterm group were wearing hearing aids by the time of their 6-year assessment, relative to one in the full term group (p=0.16). Neurological examinations (Palisano et al., 1997) conducted at 2 and 4 years and hospital notes indicated that approximately 6% of children in the very preterm group met criteria for mild cerebral palsy, while 9% had moderate-severe cerebral palsy. In contrast, only one child in the full term group met criteria for mild cerebral palsy

Table 5.1: Clinical, Social Background and Neurodevelopmental Characteristics of Participants Born Very Preterm and Full Term

	Group			
	Preterm (n=103)	Full term (n=108)	t/χ^2	p
Early Clinical Characteristics (Birth)				
M (SD, range) Gestational age	27.87 (2.38, 23-33)	39.51 (1.19, 36-41)	42.28	<0.001
M (SD, range) Birthweight	1066.63 (316.27, 385-1790)	3574.58 (409.84, 2690-4630)	48.83	<0.001
% Male	51.5	54.6	0.21	0.64
% IUGR	10.7	1.0	9.25	0.002
% Twin	34.0	3.7	31.58	<0.001
N (%) <28 weeks GA	42 (40.8)	-		
N (%) ELBW (<750g)	43 (41.7)	-		
M (SD, range) length of hospital stay	77.41 (27.94; 37-184)	-		
Respiratory support				
N (%) CLD	35 (34%)	-		
M (SD, range) Days of IPPV	6.52 (12.81; 0-62)	-		
M (SD, range) Days on CPAP	16.79 (18.16; 0-72)	-		
Evidence of Infection				
Chorioamniotis	8 (8.1)	-		
N (%) Maternal fever	10 (10.4)	-		
N (%) Antenatal antibiotics	38 (36.9)	-		

Table 5.1: Clinical, Social Background and Neurodevelopmental Characteristics of Participants Born Very Preterm and Full Term

	Group			
	Preterm (n=103)	Full term (n=108)	t/χ^2	p
N (%) Proven sepsis in infant	30 (29.1)	-		
Steroid administration				
N (%) Maternal antenatal steroids	86 (83.5)	-		
N (%) Postnatal steroids	11 (10.7)	-		
Other Medical Conditions				
N (%) ROP	37 (35.9)	-		
N (%) NEC	7 (6.8)	-		
N % PDA	46 (44.7)	-		
Neurological Characteristics (term)				
N (%) Grade 1/II IVH	23 (22.7)	-		
N (%) IVH>2	5 (5)	-		
N (%) PVL	5 (5)	-		
Social background factors (term)				
M (SD) SES[a]	3.60 (1.64)	2.82 (1.28)	2.81	0.006
% Income below NZ$ 25000 per year	18.4	8.6	4.35	0.04
% Mother left school between 13-16 years	39.8	19.4	10.06	0.002
% Maternal Age <25 at term	12.6	9.3	0.58	0.45

Table 5.1: Clinical, Social Background and Neurodevelopmental Characteristics of Participants Born Very Preterm and Full Term

	Group			
	Preterm (n=103)	Full term (n=108)	t/χ^2	p
% Maternal smoking during pregnancy	38.2	15.5	13.04	<0.001
% Minority ethnicity[b]	10.8	1.9	7.12	0.008
% Single parent at term	18.4	11.2	2.12	0.14
% Experienced change in parent	30.0	20.4	2.65	0.10
Neurosensory Impairment (6 years)				
% Legally blind	1	0	1.06	0.30
% Lenses for corrected vision	15.5	7.4	3.45	0.06
% Using hearing aid	3.9	0.9	1.99	0.16
Motor Impairment (6 Years)				
% Required mobility aid (6 yrs)	4	0	4.3	<0.05
% No CP (2yrs)	85.1	99.1		
% Mild CP	5.9	0.9		
% Moderate CP	3.0	0		
% Severe CP	5.9	0	14.64	0.002

Note. As some children were transferred from other hospitals, data from delivery or the early perinatal course was not available for all. Therefore, numbers were slightly lower than for the whole sample.
[a] Measured by Elly-Irving scale (Elly & Irving, 2003). Higher code indicates lower SES.
[b]Of these children, 6.9% in the very preterm and 1.9% in the full term group were of Maori ethnicity.

5.3 Settings

In all possible circumstances, families attended the 6 year developmental assessment at a custom-equipped research facility on the campus of the University of Canterbury. This research facility is wheel-chair accessible and has a number of rooms available for assessment. There is also a waiting room, where parents and families can view their children through a closed circuit television. The primary assessment room is fitted with a number of recording cameras, allowing for manipulation of camera angles and zoom lenses. A two-way mirror also enables researchers to view assessments from an adjacent room. Participant children sat opposite the researcher at a large table in the centre of the main assessment room for most of the tasks.

In some cases (n=10 very preterm and 6 full term children), parents were unable to travel to the assessment facility or expressed a preference for the assessment to be completed at the child's home. In these cases, the assessment was completed at a table in a quiet part of the child's home. Participants who travelled from outside of Christchurch were compensated for their travel costs.

5.4 Procedure

Within two weeks of the 6^{th} birthday (full term group) or expected delivery date (very preterm group), each child's parent was telephoned or contacted in person and provided with a verbal explanation of the study. Parents who agreed to participate were invited to an appointment at the research facility on the university campus and sent an information sheet in the mail, detailing the aims and ethics conditions of the study. If children wore glasses or a hearing aid, parents were asked to bring these to the assessment. Upon arrival at the research facility, parents were provided with a detailed explanation of the assessment procedure, reminded that all information was confidential and that they were free to withdraw from the study at any time, and given the opportunity to ask any questions before signing a consent form. Additionally, oral assent from children was acquired by asking if they were happy to participate in some activities with the assessor while their parent was interviewed. One research assistant then assessed the child while the other research assistant interviewed the parent in a separate waiting room. In the case of twins, two examiners administered tasks simultaneously in two separate rooms. Rooms were changed during a break in the middle of the session. A third person from the Child Development Research Group administered the interview to the parent.

The entire assessment lasted for approximately two hours, with a break and a snack offered after the first hour. During this break, children's height and weight were measured. However, if a child tired quickly, the assessment was stopped and another visit was organized. This occurred infrequently as there was a large variation in the types of tasks administered. After each task, the child was invited to choose a sticker. At the end of the assessment, children were rewarded with a small toy costing less than $5.00.

The tasks employed for the purpose of this study were administered in a fixed order, as follows: 1) the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R; Wechsler, 1989) 2) the Detour Reaching Box (Hughes & Russell, 1993), 3) The Visual Search (Korkman, 1990), 4) the Digit Span Test (Wechsler, 2003), 5) The Corsi Blocks (Milner, 1971), 6) The Tower of Hanoi (Simon, 1975), 7) Woodcock-Johnson III – Maths fluency, h) Woodcock-Johnson III – Passage completion, 8) Woodcock-Johnson III – Understanding Directions (Woodcock & Mather, 1989), 9) The Conner's Kiddie-Continuous Performance Task (Connors & MHS, 2001). The procedure for the administration of each of these tasks is described below. All children's assessments were recorded on DVD and video cassette so that they could later be coded and scoring checked.

In addition to these tasks, the parent completed a detailed interview to obtain information regarding family circumstances, child health and development and executive function. After the assessment, researchers completed a consensus rating of the child’s executive behaviour during the tasks and teachers were sent a questionnaire. All measures and procedures for this study were approved by the Canterbury Regional Ethics Committee (Christchurch, New Zealand, Ref. CTB/04/11/212). A detailed description of all study measures is provided below.

5.5 Measures

Measures for this study included a standardized IQ test to assess general cognitive function (IQ), several novel measures of executive function, selected to be developmentally appropriate and assess various aspects of executive control, and standardized measures of academic achievement in reading, mathematics and language comprehension. Laboratory measures were supplemented by parent and teacher reports of executive function and teacher reports of children’s academic progress relative to their class peers.

In addition to the measures obtained at 6 years of age, the longitudinal design of the study allowed for the consideration of several measures of antecedent risk. The first two sets of these measures applied for the very preterm group only and included measures of children’s early medical experiences and neurological development. A third set of antecedent factors applied for both the preterm and full term children and included early socio-familial background characteristics such as maternal age at term, marital status, SES and maternal psychological wellbeing. Finally, information about children’s early parenting experiences was available in the form of video-coded interactions between parents and children at ages 2 and 4 years. Information about the neurological status of children was available from earlier neurological assessments performed at ages 2 and 4 years.

5.5.1 Measure of General Cognitive Ability – The Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) Short Form

The Wechsler Preschool and Primary Scale of Intelligence-Revised (Wechsler, 1989) is a standardised measure of intellectual ability suitable for use with children aged 3 years to 7 years, 3 months. The WPPSI-R was ideal measure for the current study because, at 6 years of age, it is a better measure of IQ than the WISC in children with lower abilities, but remains a valid measure of IQ in children of average ability (Sattler, 2001).

Given the focus on novel measures of executive function in this study, a short form of the WPPSI-R, incorporating the 1) Picture Completion, 2) Comprehension, 3) Block Design, and 4) Arithmetic subtests was employed to provide an estimate of cognitive ability for each participant. The Picture Completion subtest assesses the ability to discriminate visual completeness by identifying missing visual details from line drawings. The Comprehension subtest assesses the ability to answer common-knowledge or logical questions using reasoning and experience. The Block Design subtest assesses visuo-spatial integration and synthesis, requiring children to reconstruct patterns using blocks, while the Arithmetic subtest assesses mental computation, requiring the child to answer verbal addition and subtraction problems without the use of paper. This test requires less than 30 minutes for administration. Average internal reliability coefficients for each of the subtests range from 0.8-0.85, while test-retest reliability ranges from 0.71 for arithmetic to 0.82 for picture completion (Sattler, 2001).

This short form of the WPPSI-R is recommended because the dyad of Block Design and Picture Completion has the highest correlation with performance IQ

(0.84), while Comprehension and Arithmetic also have a high correlation with verbal IQ (0.86) and retain a greater variety of reasoning skills than other verbal subtest combinations (LoBello, 1991). This short form has also been found to correlate highly (0.90-0.92) with full-scale IQ (LoBello, 1991; Tsushima, 1994). Split half reliability is excellent (0.93-0.94; LoBello, 1991; Tsushima, 1994) and similar to the reliability of the full form of the WPPSI-R. Factor analysis also indicates that these four particular subtests have the highest loadings with a composite intellectual factor (‘g’). Although the specificity of the comprehension and arithmetic subtests is not adequate enough warrant the interpretation of specific abilities, they nonetheless provide good measures of general verbal and full-scale intelligence (Sattler, 2001).

Several studies of preterm-born cohorts have employed the WPPSI in assessments between the ages of 5 and 7 years (Bohm et al., 2002; Bohm et al., 2004; Jakobson, Frisk, Knight, Downie, & Whyte, 2001; Roussounis, Hubley, & Dear, 1993; Sranes et al., 1997) and these have shown consistent differences in the scores of children born very preterm and full term children, indicating that the tests has good discriminant validity to detect differences in this population (Bohm et al., 2002; Bohm et al., 2004; Jakobson et al., 2001; Roussounis et al., 1993).

5.5.2 Measures of Executive Function

Several measures of executive function were administered for the purposes of this study. These measures were chosen because an extensive literature review had indicated that they reflected a broad range of executive domains, were suitable for use with children and had shown good discriminant and ecological validity in the assessment of children with neuropsychological impairment or learning difficulties. A brief overview of executive measures included in this study is provided in Table 5.1.

Table 5.2: Measures of Children's Executive Function Administered at Age 6 Years

Measure	Description	Construct assessed	Variables
Digit Span - forwards and backwards (Wechsler, 2003)	Child repeats progressively longer sequences of digits until maximum capacity is reached.	Verbal short-term and working memory	Number of trials passed (Raw score) Longest sequence of digits recalled (Span score)
Corsi Blocks – forwards and backwards (Milner, 1971)	Child must recall progressively longer sequences of highlighted blocks.	Visuo-spatial short-term and working memory	Number of trials passed (Raw score) Longest sequence of digits recalled (Span score)
Tower of Hanoi (Simon, 1975)	Disks are re-arranged to produce a goal state while adhering to rules	Planning and problem-solving	Total Score Rule breaks
Visual Search (Korkman, Kirk, & Kemp, 1998)	Child searches for visual stimuli amongst an array	Selective attention Planning	Time to complete % omission errors % commission errors Overall accuracy (Correct responses – incorrect responses)
Detour Reaching Box (Hughes & Russell, 1993)	Switch-operated box that requires the utilization of different strategies to acquire a ball	Shifting/attentional flexibility Inhibitory control (direct reaches)	Number of perseverations (shift errors) and number of direct reaches (inhibitory control errors) at each phase Pass/fail of each phase
Kiddie-Connors Performance Test (Connors & MHS, 2001).	Child must respond to a series of stimuli on a computer screen and inhibit a response to one of the items.	Processing speed (reaction time) Inhibitory control (commission errors) Sustained attention (omission errors)	Mean reaction time % Commission errors % Omission errors Overall accuracy

BRIEF – parent and teacher versions (Gioia, Isquith, Guy, & Kenworthy, 2000)	Questionnaire measure of executive behaviours in everyday activities	Executive function in everyday settings	Total working memory, inhibitory control, shifting, self-monitoring, emotional control, organisation and planning scale scores Total Metacognition Index score Total Emotional Regulation score Global Executive Composite
Behavioural rating	Custom-written rating scale	Initiation Inhibitory control Sustained attention Self-monitoring Strategic behaviour/problem-solving	4 point ratings on each measure

5.5.2.1. The Digit Span Task

Description. A Digit Span task (Wechsler, 2003) was employed to measure verbal short term and working memory. This task is widely used to assess these constructs, with forward digit span being used to assess the phonological loop, while backward span provides a measure of executive function, in that it involves the simultaneous storage and manipulation of verbal information (Alloway, Gathercole, Willis, & Adams, 2004; Gathercole & Pickering, 2000; Gathercole et al., 2004; Rosenthal, Riccio, Sanger, & Jarrat, 2006). The protocol for this Digit Span test was adapted from the Wechsler Intelligence Scale for Children (WISC-R; Wechsler, 2003). The Digit Span test is part of the working memory composite of the WISC-R and comprises two subtests – a backward and a forward span test. The advantage of measuring both spans is that the forward span can be used as a control measure of short term phonological memory and attention, while the backward span also reflects more complex working memory ability in that successful responses involve the mental reversal of the number series (Conklin et al., 2007; Lezak, Howieson, & Loring, 2004; Pickering & Gathercole, 2004).

Administration. The researcher introduced this test by telling the child that they were going to play a copy-cat game. She asked the child to copy what she said. She then introduced two practice trials of one digit each. After two administrations of one-digit trials, the span level increased. Each digit span level consisted of two trials of the same length of digit sequences, but with different numbers. The maximum number of digits administered was eight. If the child failed the task on two consecutive trials of the same digit length, the task was discontinued and the researcher proceeded to the backward sequence trials.

The backward trials were administered in the same way, except that the child was asked to speak “backwards language” and repeat the numbers backwards. Two demonstration trials of 2 digits were used to assess the child’s understanding of task requirements. If the child failed to grasp the concept of saying the numbers in reverse, the experimenter wrote the numbers on a piece of paper and showed the child that she wanted them to say these numbers in the opposite way to how they were written. If, after several attempts and corrections, the child still did not understand this concept, the task was discontinued. Otherwise the task continued until the child failed on two successive trials of the same length of digits.

Although raw scores and age-standardized scores are available for this test, the primary variables of interest for this study were the highest sequence of digits the child could correctly repeat in order (the span score) and the highest number of trials passed on the test (the raw score). This allowed for comparison between the forward and backward scores, which offers an opportunity to examine working memory as opposed to short-term memory abilities. Previous research with clinical and non-clinical populations has indicated that these scores reflect different abilities (Gathercole et al., 2004; Hale, Hoeppner, & Fiorello, 2002; Rosenthal et al., 2006). Furthermore, span scores on the Digit Span test allowed for more direct comparison with scores from the visual-spatial span test, the Corsi Blocks.

The Digit Span test has demonstrated high internal reliability, and test-retest reliability (Strauss et al., 2006). Digit span tests have been used in numerous studies of children's executive function (e.g. Brocki & Bohlin, 1999; Bull & Scerif, 2001) and have been found to correlate well with academic achievement (D'Amico & Guarnela, 2005; Jackson, Donaldson, & Cleland, 1988).

5.5.2.2 The Corsi Blocks Task

Description. The Corsi Blocks task (Milner, 1971) was used to assess spatial working memory as a complement to the Digit Span test of verbal working memory (Berch, Krikorian, & Huha, 1998; Nichelli, 2001). As shown in Figure 5.4, the apparatus for this task consisted of a wooden board measuring 27 x 20 cm, painted white and with nine wooden cubes (3 x 3 x 3 cm) arranged across the surface in non-symmetrical fashion (Milner, 1971). For ease of administration, cubes were numbered on the side facing the examiner.

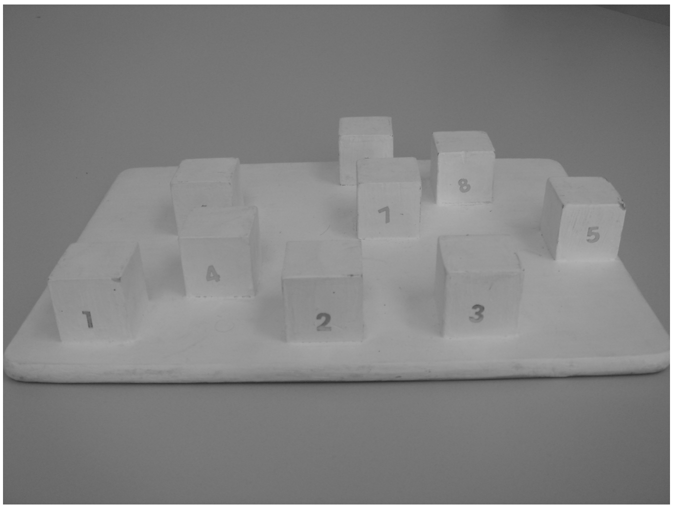


Figure 5.4: The Corsi Blocks Task

Administration. The examiner placed this apparatus in front of the child and stated, “Now we are going to play another copy-cat game, but this time, I want you to wait until I finish and then copy my pointing.” Then the examiner demonstrated by pointing to one block with her index finger and asked the child to do the same. Two practice trials of 2 blocks were administered. Between successive blocks, the researcher placed her fist back on the table. This ensured a more standard time interval between successive blocks. The span trials progressed in the same way as the Digit Span trials. Consistent with the Digit Span trials, the criterion for cessation of administration was the failure of two successive administrations of equal span length.

For the backwards sequence trials, the administrator asked the child to copy her tapping again, but to point to the blocks in reverse order. That is, so that the last one that the researcher touched would be the first that the child touched. Two demonstration trials were administered. If the child did not grasp the concept of pointing in backward order or continued to point in forward sequence after repeated explanation, the task was stopped. Trials proceeded in the same way as those on the forward-span task, with two incorrectly completed sequences of the same length being the criterion for cessation. The number of trials that the child managed to pass was recorded as the raw score. The longest level of digits correctly repeated was recorded as the span score.

Variations of the Corsi Blocks Task have been used in the assessment of working memory across a range of age groups and with different clinical populations (e.g. Berch et al., 1998; Fischer, 2001; Gathercole, Tiffany, Briscoe, & Thorn, 2005). Furthermore, the Corsi Blocks Task has been shown to be age sensitive (Isaacs & Vargha-Khadem, 1989; Nichelli, 2001), as well as sensitive to neurological damage, particularly to the right hemisphere, in adults (Kessels, Zandvoort, Postma, Kapelle, & de Haan, 2000; Lezak et al., 2004). Previous studies have also indicated that older preterm children show deficits on a computerized block-tapping task (Luciana et al., 1999; Taylor et al., 2004). There is evidence that the critical faculty that this task taps is the ability to construct and recall mental path configurations between the blocks, suggesting that this task is ideal for assessing spatial processing abilities. However, factors such as attention and the ability to devise a strategy may also have an influence on Corsi Blocks performance (Berch et al., 1998; Fischer, 2001).

5.5.2.3 The Tower of Hanoi

Description. The Tower of Hanoi (Simon, 1975) disk transfer task is a popular measure of neuropsychological function and particularly of frontal lobe processing (Welsh, Saterlee-Cammel, & Stine, 1999). It was used to measure planning processes and problem solving in this study. Most researchers concur that the Tower Hanoi task is a measure of planning and problem solving, in that disks need to be transferred to a goal position in the fewest number of moves possible while abiding by a set of constraints. Thus, the participant must plan the sequence in advance, employing working memory to hold rules and constraints in mind (Ahonniska, Ahonen, Aro, Tolvanen, & Lyytinen, 2000; Goel, 1995; Welsh et al., 1991). However, it has also been argued that inhibitory control is involved in successful completion of this task since the respondent must resist placing the first disk in the most intuitively obvious position and initially move disks away from the goal position in order to successfully complete the task (Fireman, 1996). Consequently, the Tower of Hanoi is often referred to as a complex executive measure (Miyake et al., 2000; van der Sluis et al., 2004)

The Tower of Hanoi apparatus consists of a platform with three pegs. For this study, two identical platforms were made from rectangular pieces of wood, approximately 30cm long and 9cm in width. The pegs, all 11cm in length, were equidistantly positioned in a straight line down each block of wood. Disks of graduated sizes and approximately 1cm deep were also constructed of wood and painted in different colours. These disks could be moved comfortably from one peg to another in order to construct a target configuration.

Administration. The researcher used one apparatus with three disks to explain the rules of the task, demonstrating and using visual emphasis to indicate what was not allowed. The rules were as follows: First, a disk could not be placed on the side of the platform or on the table, but could only be on the resting pegs or in hand. Second, a larger disk could not be placed on top of a smaller one. Third, only one disk could be removed at a time (Welsh & Huizinga, 2001). The researcher checked the child’s understanding of task rules by asking them to repeat what they were or were not allowed to do.

There were 12 trials in this task, four requiring a 2 disk configuration, four requiring 3 disks and four requiring 4 disks. The various start and goal positions for each trial are illustrated in Appendix B. The first trials necessitated only two moves in order to be completed optimally. Like the 2-move task administered by Khlar and Robinson (1981), this move level did not require the child to overcome any obstacles, but only to obey rules and perform moves in the correct sequence. The researcher set up the desired design on her apparatus and the start design on the child's apparatus, telling the child to close their eyes as she did this. She placed both on the table and said, "Open your eyes." Then, pointing to the desired configuration, she said, "I want you to make your tower look the same as mine on this peg in as few moves as possible. Remember the rules." Each trial was coded dichotomously (pass/fail) according to whether the child completed the task in the given number of moves without breaking rules. As well as this, the number of moves (planning proficiency) that the child took and the number of rule breaks (inhibitory control) were recorded. Each pattern was completed on reverse sides and children were allowed an unlimited amount of time to complete the task. Similar to the procedure adopted by other researchers (Bishop, Aamodt-Leeper, Creswell, McGurk, & Skuse, 2001; Carlson, Moses, & Claxton, 2004), if the child was unable to complete a move level within 2 consecutive trials, the task was terminated. However, if a child did break a rule, he or she was gently reminded after completion to remember the rules they had been taught. Another disk was added if the child passed the first four trials, making the shortest number of moves 5. A fourth disk was added if the child was able to reach the 9-move task. Few children succeeded in completing the 10-move task and no further trials were administered after this. The number of correctly passed trials was added to create a total Tower of Hanoi Task score (Emick & Welsh, 2005).

Humes, Welsh, Rezlaff and, Cookson (1997) found that the Tower of Hanoi has high internal consistency, with a split half reliability of 0.87 and correlations between individual trial scores and the overall task scores ranging from 0.68-0.81 in adults. In support of its construct validity, performance on the Tower of Hanoi has been found to correlate with other tests of various domains of executive function (Humes et al., 1997; Welsh et al., 1999).

The discriminant validity of the Tower tasks for measuring neurodevelopmental integrity is supported by a number of studies that show that performance on this task is impaired in adults and children with neurological injury, particularly in the prefrontal cortex (Goel, 1995; Levin et al., 1994; Owen, Morris, Sahakian, Polkey, & Robbins, 1990). This is the case even when differences in IQ are accounted for, suggesting that the task may be especially sensitive to frontal cortex function (Goel, 1995) Additionally, performance on the Tower of Hanoi is generally impaired in populations believed to have neuropsychological deficits. For example, scores on the Tower of Hanoi have been shown to discriminate children with ADHD (Kopecky, Chang, Klorman, Thatcher, & Borgstedt, 2005), PKU (Welsh, Pennington, Rouse, & McCabe, 1990) and Autism (Ozonoff & Jensen, 1999) from children without clinical diagnoses.

5.5.2.4 Visual Search

Description. The Visual Attention subtest from the attention/executive function scale of the NEPSY (Korkman et al., 1998) was used to measure selective visual attention. The NEPSY is a standardized measure of neuropsychological functioning. The Visual Attention subtest measures the ability of the child to selectively isolate target stimuli within an array. Two trials were administered. For the first trial, 20 black and white pictures of cats were randomly arrayed amongst 80 pictures of items such as apples and trees. An example target picture was shown at the top of the A3 page. The items in this array were approximately 2 cm in height and width. In the second, more complex trial, a male and a female face were shown at the top of the

A3 page. Children had to identify these faces (10 of each) from an array of 55 distracter faces that often differed only slightly from the stimulus faces. The two target items were not paired within the array so that children were effectively conducting a search for two separate target items at the same time. The pictures in this array were approximately 2.3-3 cm in height and width. All pictures were printed in black and white.

Administration. The page was placed in front of the child on the table top. The examiner pointed to the target item at the top of the page and asked, “What is at the top of this page?” Once the child had correctly responded, the examiner asked the child to find all of the target items on the page and demonstrated how to mark the item by making a cross through the item with a pencil. The child was asked to find all the target items as quickly as possible and to let the examiner know when they were finished. The examiner then timed the task as the child completed it. Where children made obvious errors, such as crossing out all items on the page, the examiner gently gave one reminder that they were only to cross off the target items. For the second ‘faces’ search trial, the child was shown the two faces at the top of the page and told to find all of the faces that looked exactly the same as either of the faces at the top of the page. The child was also told that the two faces did not have to be next to each other. According to standard protocol, the examiner indicated that the child should search all of the rows and say when they had finished searching. As soon as the child began searching, the examiner started a stopwatch. After 180 seconds, or when the child notified the examiner that they had finished searching, timing was ceased.

The NEPSY Visual Attention subtest has been standardized for use with 5-12 year olds on samples from the USA and Finland. Outcome scores include an accuracy score, which reflects the number of correct-incorrect responses for the trials administered, mean time to search, a raw score, derived from the accuracy and mean time to search, and a standardized score according to the test norms. Standardised scale scores have a mean of 10 and a standard deviation of 3 (Korkman et al., 1998).

The NEPSY is based on neuropsychological theory, and in particular on the work of Luria (1973). Content validity was assessed via a panel of experts across the United States (Haynes, 2001). Mean-test-retest reliability for the Visual Search task of the NEPSY is 0.71 and the task has been shown to be developmentally sensitive to age differences in a large sample (n=800; Korkman, Kemp, & Kirk, 2001). The Visual Attention subtest has also been shown to have discriminant sensitivity to neurological and scholastic difficulties (Schmitt & Wodrich, 2004) and has been significantly related to the rate of acceleration in mathematics performance across the first three years of school (Aunola, Leskinen, Lerkkanen, & Nurmi, 2004).

5.5.2.5 The Detour Reaching Box

Description. The Detour Reaching Box (Hughes & Russell, 1993) was used to measure attentional set shifting and inhibitory control. The task requires the participant to replace a prepotent response (a direct reach) with another simple action (turning a knob or pressing a switch) in order to accomplish a goal (obtaining a ball from the box). The Detour Reaching Box is shown in Figure 5.5. The apparatus consisted of an aluminium box (30cm x 30cm x 30cm) with a circular window through which the child could reach in order to obtain a ball from a square platform. When the researcher activated a sensor, however, reaching directly through the window into the box caused a small trap door in the platform to open and the ball dropped out of sight. Two lights were visible to the child at the front of the box. When there was no light, the child could reach into the window and obtain the ball directly. When the light was yellow, the child had to turn a dial on the right hand side of the box to project the ball down a ramp. When the light was green, the child had to use a switch on the left hand side of the box to deactivate the sensor and retrieve the ball. Thus, depending on the light cue, one of three different strategies could be used to obtain the ball.

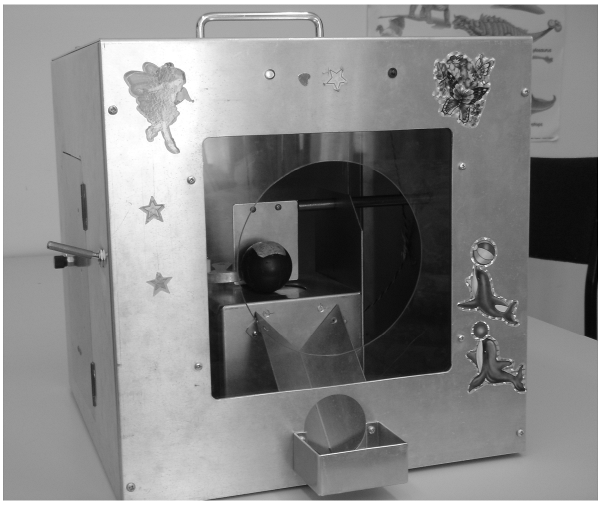


Figure 5.5: The Detour Reaching Box

Administration. There were four phases to this task. During the first *direct route phase*, the experimenter allowed the child to reach into the window and obtain the ball. Once the child had successfully retrieved the ball on three successive trials, the task proceeded to the second *yellow light phase*. The experimenter pointed out that the light on the box was now yellow and showed the child how to access the ball using the dial on the right hand side of the box. Each time she replaced the ball, the researcher asked the child, “What colour is the light? How do I get the ball when the light is yellow?” Again, the child was required to demonstrate that they could successfully retrieve the ball three times in order to move to the subsequent phase. If a child had not managed to reach the criterion after 15 trials, the task was discontinued. Similarly, during the third *green light phase* of the task, the child had to obtain the ball three times by using the switch on the left hand side of the box. During the fourth, *alternating phase* of the task, the lights were activated in an alternating pattern so that the child had to use the light to select the correct strategy to obtain the ball. Eight trials were administered during this phase. Across all phases of the task, the researcher recorded the number of direct reach errors, switch errors (i.e. trying to use the knob when the light was green or vice versa) and motor control errors (not grasping the switch firmly enough or not holding it down long enough to retrieve the ball).

Although the Detour Reaching Box task has not been used extensively, studies do support its utility in the measurement of executive strategies. The Detour Reaching Box was originally developed and used by Hughes to examine executive processes in children with Autism (Hughes & Russell, 1993) and with hyperactivity/antisocial behaviour (Hughes, Dunn, & White, 1998) in comparison to control groups. The task demonstrated discriminant validity in both studies. These children tended to perseverate with unhelpful strategies, highlighting the task's utility in measuring executive processes (Hughes & Russell, 1993). The box task was also shown to be age sensitive, with older children requiring fewer trials to master the task (Hughes et al., 1998).

Hughes (1998) has shown that children's performance on the Detour Reaching Box correlates moderately ($r = 0.38$-0.69) with other executive function tasks such as the Tower of London, an inhibitory control and a working memory task. In a separate study, poorer performance on the Detour Reaching Box was also found to correlate with antisocial behaviour in preschool children, suggesting a relationship with behavioural regulation (Hughes, White, Sharpen, & Dunn, 2000). The task has also been used previously in the present sample at age 4 years, where children born very preterm were found to have greater difficulty than their peers in flexibly alternating between strategies (Edgin et al., 2008).

5.5.2.6 The Conner's Kiddie-Continuous Performance Test

Description. Originally developed to study vigilance in adults with brain injury and epilepsy (Connors & MHS, 2001; Mahone, 2005), continuous performance tests are widely used to measure sustained attention and inhibitory control in adults and children. Adapted from the well-validated adult Conner's Continuous Performance Test (Connors, 1995), the K-CPT (Connors & MHS, 2001) was standardized on a set of 314 children with no clinical diagnoses and 100 children diagnosed with ADHD aged 4 to 5 years. This task was included in the present study because of the interest in executive attention and because it makes use of familiar pictures (e.g. a horse, a house, a telephone) as opposed to the letters that are used in the adult version of the task and that may not have been familiar to some of the children. Additionally, the commercially available adult versions of the Continuous Performance Test have running times of 14 minutes or more, which was considered very lengthy, given the already demanding nature of the current assessment protocol

The running time for the K-CPT is 7.5 minutes. Children are instructed to press the space-bar in response to the presented pictures, but to refrain from pressing the space-bar when they see a soccer ball. In this respect, the K-CPT is similar to go/no go tasks, because continuous performance tasks generally require the participant to respond to one item and not to others, while go/no go tasks require a response to most items, with an inhibitory response to only one of the stimuli (Berlin & Bohlin, 2002). The interval between stimuli on the K-CPT ranged from 1500ms to 3000ms, with a display time of 500ms. The test is divided into ten blocks, with each of these consisting of a number of 1500ms trials and a number of 3000ms trials (Connors &

MHS, 2001).

Administration. This task was administered using a lap-top computer. After all other tasks were completed, the research assistant led the child to the computer and explained the task. The researcher watched to make sure the child had understood the task instructions. Pilot evaluation of this task suggested that children were likely to be distracted and talk to the researcher if she was in the room. Thus, to minimise distraction, children were told that the researcher was going to find them a thank-you present and that they should continue with the task until she returned. Following this, the researcher left the room and could monitor the child through a one-way mirror in the adjacent area. If the child got up from the chair, the researcher returned to the room and encouraged the child to go back to the task.

Measures of children's performance on the K-CPT included reaction times, the percentage of errors of omission (failure to press the space bar for a target), the percentage of errors of commission (pressing the space bar when non-target soccer ball was on the screen) and the percentage of perseverative errors (responses before 100ms). Fast reaction times with many commission errors and few omission errors are indicative of more impulsive responding, while slow reaction times with many omission errors tend to reflect inattention (Connors & MHS, 2001).

Split-half reliability coefficients of the K-CPT outcome measures for children between 4 and 5 years range from 0.72-0.88 (Connors & MHS, 2001). In support of the validity of the test, several of the scores for the normative clinical and non-clinical samples differed significantly. In support of the discriminant validity of CPT tasks, many studies have shown significant differences in the performance of children with ADHD, with these children showing more errors of commission and slower response times, compared to children without ADHD (Barkley, 2001;

Pennington, Bennetto, McAleer, & Roberts, 1996). Using the K-CPT, Pollack, Vardi, Bechner, and Curtin (2005) also found that older children had higher hit rates and faster response times than younger children

5.5.2.7 The Behavior Rating Inventory of Executive Function (BRIEF) – Parent and Teacher versions

As a supplement to laboratory measures, the Behavior Rating Inventory of Executive Function (Gioia et al., 2000) was used to assess executive behaviour in everyday settings, as opposed to the artificial environment of the assessment laboratory. Both the parent and teacher versions were used to assess children's behaviour across different environments.

The BRIEF is suitable for children aged 5-18 years and takes 10-15 minutes to complete (Fitzpatrick, 2003). It consists of 86 items, rated on a 3-point scale from 'never,' to 'always.' Items such as, "Has trouble putting the brakes on his/her actions," assess behavioural regulation while items such as, "Does not check work for mistakes," assess metacognitive aspects of executive function. Responses are scored 1, 2 or 3 respectively, and summed to produce a number of different scale scores, which are standardised according to gender. These scales are labelled:

1. Inhibit: The ability to inhibit and control impulsive responses.
2. Shift: Flexibility in problem-solving, the ability to switch focus and the ability to transition comfortably between different activities and situations.
3. Emotional Control: Emotional lability and regulation of emotional responses.
4. Initiate: The independent generation of ideas or strategies and the ability to begin a task without significant prompting.

5. Working Memory: Holding information in mind in order to complete a task.
6. Plan/organise: The ability to set goals and develop steps to achieve them and the ability to organise language/writing.
7. Organisation of materials: Organisation of the child's desk, room, cupboard.
8. Monitor: Work checking and self-evaluation.
9. Behavioural regulation index: Consists of the summed inhibit, emotional control and shift scores and reflects the child's ability to modulate their behaviour and emotions.
10. Metacognition: Consists of summed initiate, working memory, plan and organisation of materials scores and reflects the child's executive control of cognition.
11. General Executive Function Index: Sum of all scores.

The BRIEF has been shown to be internally consistent (r = 0.8-0.98) with test-retest reliability coefficients ranging from 0.76-0.92. Inter-rater agreement between teachers and parents is moderate (r = 0.32; Fitzpatrick, 2003; Gioia et al., 2000; Schraw, 2003). Additionally, the BRIEF correlates well and in the expected direction with measures of children's behaviour, e.g. the *ADHD Rating Scale* (Du Paul, Power, Anastopoulos, & Reid, 1998), the *Child Behaviour Checklist* (Achenbach, 1991) and the *Connor's Rating Scale* (Connors, 1997; Gioia et al., 2000; Mahone et al., 2002).

The BRIEF has also been found to discriminate between typically developing children and children with ELBW (Anderson et al., 2004), ADHD (Gioia, Isquith, Kenworthy, & Barton, 2002; Mahone et al., 2002); spina bifida and hydrocephalus (Burmeister et al., 2005), brain injury (Anderson et al., 2002; Gioia et al., 2002) and reading disability (Gioia et al., 2002). As would be expected, these studies also showed that BRIEF scores for these diagnostic groups were different in terms of the extent and nature of the deficits, with children with ADHD, for example, showing lower scores on the behavioural regulation items (Mahone et al., 2002) and children with the inattentive form of ADHD showing less difficulty on the inhibitory control scale than those with the combined-type ADHD (Riccio, Homack, Pizzitola Jarrat, & Wolfe, 2006).

In the current study, Cronbach's alphas for the parent BRIEF ranged from 0.75-0.90, with those for the Behavioural regulation index and the Metacognition indexes being 0.85 and 0.87 respectively. Cronbach's alphas for the teacher BRIEF scales ranged from 0.83-0.95, with those for the Behavioural Regulation and Metacognition Indexes being 0.88 and 0.93 respectively. After repeated phone calls, school visits and reminders, 97 teacher questionnaires were obtained for the very preterm group and 104 for the full term group.

5.5.2.8 Behavioural Rating

Directly after each assessment, assessors discussed and rated executive aspects of each child's behaviour. This is in keeping with the suggestions of other researchers, who highlight the importance of using qualitative measures in conjunction with standardised testing (Gioia et al., 2001; Hughes, 2002; Strauss et al., 2006). Five aspects of executive function during children's task performance were rated on a scale of 1(low) to 4 (optimal). These included initiation, inhibition, sustained attention, self-monitoring and strategic behaviour. The rating categories for the scale were chosen to compliment the cognitive measures administered in the laboratory and are also similar to some of the BRIEF scales. The criteria for various scales are shown in Appendix C.

5.5.3 Measures of Academic Achievement

5.5.3.1 Woodcock-Johnson III

Three subtests from the Woodcock-Johnson III Achievement Battery were used to assess children's academic progress. These included:

1. *Passage comprehension*. This test is part of the reading cluster of the achievement battery and was used to assess children's early reading ability. The subtest is recommended for use with younger school aged children (Strauss et al., 2006). The test is administered with a free-standing booklet, so that one page faces the participant and the other faces the administrator. This enables the examiner to read instructions directly from the page. The test progresses from a simple test of understanding of symbols, through to reading sentences independently and inserting a correct word. Passages become more difficult as fewer pictures and more complex words are introduced. Administration of the test is ceased after eight consecutive incorrect answers. The test-retest reliability for this subtest is 0.75 (Mather, 2001).

2. *Maths Fluency*. This is a timed pen and paper test that measures a child's ability to solve addition and subtraction problems quickly. Children are given three minutes to complete the problems as quickly as possible. For the purposes of this study, the test format was revised. The original presentation is a large A3 sized sheet of problems presented vertically. Pilot investigation and consultation with local school teachers suggested that a vertical format was less familiar to younger children in New Zealand schools. Therefore, the sums were presented horizontally and the print was enlarged so that there were fewer problems on each sheet. The revised presentation sheets are presented in Appendix D. The researcher checked the child's understanding and showed

him/her where to write the solution before starting the timer. If a child completed an A4 sheet of problems before three minutes were finished, they were presented with another. Where children had severe cerebral palsy that prevented them from writing, they read the examiner the item and told the examiner their answer. The maths fluency test has a test-retest reliability of 0.95 at age 7 (McGrew & Woodcock, 2001). Scoring is based on the number of correctly completed problems regardless of the quality of children's writing. For example, if a child reversed a number, the problem was still scored correctly.

3. *Understanding Directions.* Understanding Directions is part of the oral language composite of the Woodcock Johnson III and measures a child's ability to follow oral directions by pointing to the list of items on a coloured picture. Similar to the Passage comprehension subtest, this test is administered via a standing booklet, with the pictures facing the child. The test is generally administered via auditory cassette, but instructions were spoken in this study because it was felt that children may have had difficulty with the American accent on the audio tape. The instructions for the first part of the test are simple (e.g. "Point to the monkey in the tree"), but become very complex as the test progresses (e.g. "Before you point to the picture on the right wall, point to the dog, but not the largest dog"). This subtest is recommended for younger children and has a test-retest reliability of 0.85 at age 6 (McGrew & Woodcock, 2001; Strauss et al., 2006).

The Woodcock-Johnson has been used widely used as a measure of educational achievement in children born preterm (Breslau et al., 2001; Breslau et al., 2004; Hack et al., 1992; Hack et al., 1994; Klebanov et al., 1994b; Litt et al., 2005; Taylor et al., 1998). The Woodcock Johnson-III is designed to cover an extensive age range (2-90) and was standardized on a large, randomly selected, population-representative United States sample (Cizek, 2003; Sandoval, 2003; Strauss et al., 2006). Test-re-test reliabilities have been calculated for intervals over a year and are high (0.7-0.9; Cizek, 2003; Strauss et al., 2006). Furthermore, the Woodcock Johnson-III achievement tests correlate significantly with other widely-used tests of achievement, including the *Wechsler Individual Achievement Test* and the *Kaufmann Test of Educational Achievement* (r=0.59-0.8; Mather, 2001; Sandoval, ; Strauss et al., 2006) and show expected patterns in children with learning difficulties (Floyd, Bergeron, & Alfonso, 2006; Floyd, Evans, & McGrew, 2003; Riccio et al., 2006). As part of the standardisation process, the tests were reviewed by experts for cultural bias (McGrew & Woodcock, 2001).

5.5.3.2 Teacher Ratings of Educational Achievement

Teachers were asked to rate each child's progress in three curriculum areas on a custom-written, 5-point, likert-type scale ranging from delayed to above average. These three areas included reading, mathematics and language comprehension.

5.5.4 Antecedent Clinical, Neurological and Socio-Familial Measures

In order to examine relationships between a range of specific early clinical and socio-environmental factors that may have subsequently influenced the development of executive function in children born very preterm , the following factors were identified from a larger study database.

5.5.4.1 Child Clinical Characteristics

Data related to the medical history of children born very preterm was collected throughout the perinatal period and included maternal smoking during pregnancy, intrauterine growth restriction (IUGR), maternal fever or chorioamniotis at the time of delivery, proven sepsis in the infant, ventilatory support and respiratory disorder [respiratory distress syndrome (RDS), chronic lung disease (CLD), days on CPAP and IPPV], patent ductus arteriosis (PDA), necrotizing entercolitis (NEC), retinopathy of prematurity (ROP), intraventricular haemorrhage (IVH; graded according to the Papile system; Papile, Burnstein, Burnstein, & Koffler, 1978) and periventricular leukomalacia (PVL).

5.5.4.2 Qualitative Magnetic Resonance Imaging

MRI scans of all of infants born very preterm were taken at term age equivalent (between 39-41 weeks post conception, as estimated by foetal ultrasound). Prior to scanning, infants were fed and wrapped in an inflatable, form-fitting bean bag. This helped to ensure that the infants were comfortable and still during the scan.

Images were acquired with a 1.5 Tesla General Electric Signa System scanner. Two different imaging protocols were applied. First, a fourier transform spoiled gradient recalled sequence was applied (18 cm field of view, 1.5mm coronal slices, 45 degree flip angle, repetition time 3000ms, echo time 5 ms, voxel volume 0.7 x 0.7 x 1.5mm, matrix 256 x256). Second, a double echo-spin echo sequence was performed (Proton density and spin density weighted; 18cm field of view, 3mm axial slices, interleaved acquisition, 3mm axial slices, repetition time 3000ms, echo time 36 and 162ms, 0.7 x 0.7 x 3 mm voxel volume and 256 x 256 matrix).

These scans were subsequently graded for the presence and severity of white and grey matter abnormality by a paediatric neuroradiologist who was blind to infant neonatal history (Inder et al., 2003). A second neurologist independently scored these scans and inter-rater reliability was found to be 95%. White matter abnormality was graded on a 3-point scale of 1 (not present; normal), 2 (mild/focal damage) or 3 (moderate/severe/diffuse damage) for each of the following criteria: 1) presence of cysts, 2) periventricular white matter signal abnormalities, 3) periventricular white matter volume loss, 4) ventricular dilation, 5) thinning of the corpus callosum. Grey matter abnormality was graded on a 3-point grading system for each of the following criteria: 1) grey matter signal abnormality, 2) quality of gyration of the brain according to previously reported criteria (Chi, Dooling, & Gilles, 1977; Martin et al., 1988) 3) the size of the subarachnoid space. Scores were summed to form composite indicators of white and grey matter abnormality.

5.5.4.3 Social Background and Family Functioning

Socioeconomic Status. The Elly-Irving scale of socioeconomic status (Elly & Irving, 2003) was used to assess family SES on the basis of reported profession. The highest recorded score in the household was used as the socioeconomic index. Scores range from 1 (professional) to 6 (manual/unskilled labour), with unemployed parents assigned a score of 7. The measure has demonstrated predictive validity in an independent study (Fergusson, 2000). The level of income in the household was also recorded at six years of age. Parents rated their income on a scale of 1 (less than $15 000 per year) to 6 (70 000 and over per year).

Maternal age. Maternal age at the time of birth was recorded in whole years.

Marital status. The mother's marital status at the time of birth was recorded as single, defacto or married.

Family Stability. This measure consisted of the total number of parental changes from birth to 6 years. Parental changes were defined as separation or divorce, the death of a parent, parental reconciliation, placement in foster or adoptive care, long-term parent prison sentences or going to live with a relative. The number of these changes was added for each child across birth to 6 years.

Parental Depression/Anxiety. The Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) was used to assess symptoms of depression or anxiety in mothers. This 14-item measure consists of statements such as; "I feel as if I'm slowed down," and "I get sudden feelings of panic," which mothers rated on a scale of 0 (never) to 3 (most of the time). Scores are summed to produce composite indexes of depression and anxiety. Scores above 11 indicate clinically relevant signs of depression or anxiety, while those above 8 indicate borderline levels of clinical depression and/or anxiety (Zigmond & Snaith, 1983). The HADS has been used as a screening tool across international samples (Herrmann, 1997). Psychometric evaluations indicate that test re-test reliability is high (r = 0.8) and internal consistency for each of the scales is excellent (0.68-0.90). The HADS is sensitive to mood disorders in various populations and is sensitive to changes in mood over time (Bjelland, Dahl, Haug, & Neckelmann, 2002; Herrmann, 1997; Martin, Bonner, Brook, & Luscombe, 2006; Mykletun, Stordal, & Dahl, 2001; Raeder, Steen, Vollset, & Bjelland, 2007). Sensitivity for depression and anxiety has ranged from 70-90% in studies that have used a cut-off criterion of 8 (Bjelland et al., 2002). For the purposes of this study, the number of depressive and anxious episodes from 1 to 6 years was recorded.

Family Life Event Stress. Assessment of the extent of family stress due to challenging life events was based on the Social Readjustment Rating Scale (Holmes & Rahe, 1967), but differed in that participants were able to nominate their own stress levels regarding an event, as opposed to using a point system. Parents were asked about a number of familial experiences, spanning marital conflict or separation, pregnancy, miscarriage, financial issues, changes in living circumstances, unemployment, illness, injuries, deaths and legal issues. As well as asking if these events had occurred, parents were also asked to rate how stressful they felt the experience to be on a scale from 1 (not upsetting or stressful) to 5 (very upsetting). The number of events was multiplied by the level of stress to form a composite measure of stressful life experiences from 1 to 6 years.

Early Parenting. At ages 2 and 4 years, a structured parent-child play interaction, based around a series of problem-solving tasks, was completed. Interactions were described to parents as an opportunity to see how children learned to solve problems with the support of someone familiar and were video-taped for subsequent coding. The procedure was similar across both ages. Before beginning the activity, each problem-solving task was explained and parents were shown how to complete the task while another researcher distracted the child with a toy. Parents were instructed to introduce and complete each task one at a time and to allow the child a few minutes to explore each task by themselves before offering assistance. Following this time, parents were told that they were free to provide whatever assistance they deemed necessary to help their child complete the task. Once the parent indicated that they understood the procedure, the researchers left the room and video recording began.

Three different, age-appropriate problem-solving tasks were used at each assessment point. The tasks used at both ages were similar in nature, but differed in complexity to offer appropriate developmental challenge. At age 2 years, parents and children completed three activities. The first was a colour-matching puzzle, which involved matching twelve coloured disks to their corresponding colour on a puzzle board. The second task required the child to slide a sliding lid on the top of a two-holed (triangle and rectangle) posting box and then place each shape in the corresponding posting hole. The third activity involved a more complex task using a clear rectangular perspex box (Matas, Arend, & Sroufe, 1978). A small smiley-faced stamp was placed within the box and the child had to place a weight on a wooden lever to lift the stamp and retrieve it.

At age 4 years, children completed four tasks. The first task was a simple, ten-piece jigsaw puzzle of a teddy bear. The second activity was a magnetic letter-board, requiring children to copy the word ‘flower’ using magnetic letters. A selection of letters spanning the whole alphabet was available, and children had to select those of the same colour to match on the board. The third activity required children to a copy a castle model using large Lego blocks and the fourth was a bead-threading task in which children were required to reproduce a pattern of threaded beads of different colours and shapes. The activities were hidden with cloth covers so that parents could introduce each activity one at a time.

Similar to previous studies (Mize & Pettit, 1997), a range of child and parent behaviours were coded based on these videotaped parent-child interactions. Raters coded child behaviours first, then rewound the tape to code maternal behaviours during the interactions. For each problem solving task, parent behaviours were rated using five 5-point likert-type scales from 1(low) to 5 (high). The following three subscales were selected for inclusion in this study:

Parental supportive presence included verbal and non-verbal behaviours such as leaning in towards their child when they were having more difficulty, being involved and encouraging, providing assistance in a timely fashion, pacing the interaction so that the child remained engaged or allowing the child to explore the puzzles while anticipating when they required more support.

Parental intrusiveness included excessive or inappropriately controlling behaviour. Parents who used dictatorial instructions, interfered or took over task completion without allowing the child time to explore or tackle the tasks independently were rated higher on this measure.

Parent-child interactional synchrony included responsive, reciprocal and mutually-guided behaviour such as eye gazing, shared affect, being responsive to partner cues, maintaining a mutual attentional focus, peer-like behaviours or mirroring each other's affect. Behaviours that were not reciprocal included incidences where one partner abruptly changed the focus of the interaction, missing cues, irrelevant comments, or non-contingent behaviours.

Trained raters (two and 2 years and three at 4 years) independently coded tapes for 2 and 4 year interactions using the same methods and coding system. Inter-rater agreement was assessed for absolute agreement for 15% of tapes at 2 years and 20% at 4 years. Intra-class correlations were 0.84 for parental sensitivity, 0.74 for intrusiveness and 0.88 for interactional synchrony at age 2 years. At age 4 years, intra-class correlations were 0.78 for supportive presence, 0.82 for intrusiveness and 0.84 for interactional synchrony. Scores for each age were meaned to form a composite measure across time points.

5.6 Data Control and Analysis

5.6.1 Statistical Power

With a sample size of approximately 100 in each group, it is possible to detect, with 80% power, effect sizes • 0.4 at a significance level of $p<0.05$. The power drops to 68% for an effect size of 0.3 (Cohen, 1988). For dichotomous Chi-squared tests with 1 degree of freedom, a sample of 100 is sufficient to detect group difference effects of 0.3 at 80% power and $p<0.05$ (Cohen, 1988).

5.6.2 Statistical Methods

Data was analysed using the Statistical Package for the Social Sciences (SPSS) 15.0. Analysis was conducted in four stages, according to the study aims. Initial analyses were completed for all children born very preterm and full term who had participated in the 6-year follow up study. During the first stage, data was explored using frequency tables, scatter plots, histograms and box plots in order to identify outliers or missing values and to examine the respective distributions across each group. Descriptive statistics, including t-tests and Chi-squared tests were completed for dependent measures, with follow-up non-parametric tests completed to ensure that findings were robust after the consideration of distribution properties. A p-value of $p<0.05$ was used as the cut-off criterion for statistical significance for these initial statistical analyses. All descriptive analyses were repeated excluding children with cognitive delay (IQ<70) and/or moderate to severe motor impairment. Given that groups differed in SES, group differences on continuous measures were further explored using analysis of covariance (ANCOVA) with SES entered as a covariate. Group differences on bivariate outcome measures were analysed using logistic regression with SES entered as a covariate.

During the second stage of data analysis, the extent of convergence of executive function performance across laboratory-based measures was examined for both groups of children using correlations, principle components analysis and confirmatory factor analysis. This analysis allowed for data reduction in accordance with the theoretical assumption that laboratory-based measures were assessing a latent executive function construct.

During the third stage of analysis, only data from the preterm group was included in order to examine the predictors of executive function performance at age 6 years. Correlations, t-tests and ANOVAs were used to examine associations between antecedent clinical, neurological and social-familial factors, with subsequent multiple regression modelling used to determine which of these were the strongest predictors in the context of multiple correlations. Because these models were aimed at describing relationships across these measures and because of the restriction of power due to the decrease in sample size, a p-value of $p<0.10$ was used for inclusion in the multivariate models.

During the fourth stage of analysis, associations between very preterm birth status, executive function performance and academic achievement measures were examined. For this final set of analyses, data from the full term group was again included. Relationships between executive function and academic achievement were examined for each group using correlations and univariate ANOVA. Multivariate models were then constructed in order to ascertain the relevance of executive function measures in accounting for group differences in academic achievement. Further details of these analyses are presented in subsequent chapters.

Chapter 6

Results 1: Cognitive and Educational Outcomes at Age 6 Years in Children Born Very Preterm and Full Term

An extensive review of the outcomes of children born very preterm suggested that these children are at risk of experiencing difficulties in a number of different domains, including general cognitive function and academic achievement. However, there are numerous limitations in the extent to which these studies can be generalised across cohorts. Furthermore, some debate continues over the extent to which differences in the mean performance of groups of children born very preterm are the result of a select group of children who perform very poorly, and thereby pull collective scores down. Finally, most studies that have focussed on children's achievement have tended to focus on older groups of children born very preterm, leading to a dearth of information about performance in the early school years, when specific intervention efforts are likely to prove most effective. With these issues in mind, this chapter describes the general cognitive and academic performance of a cohort of children born very preterm and a comparison group of children born full term at age 6 years.

This analysis was intended as a general description of the broad outcomes of these children before embarking on a more detailed description of their performance on specific neurocognitive measures in the next chapter. In lieu of this aim, bivariate descriptive statistical tests such as chi-squared tests and t-tests for independent means were used to compare group performances. Following this, the influence of selection factors such as differences in group SES were considered. These analyses were performed by including SES as a covariate in between-group ANOVA models or logistic regression models in the case of bivariate dependent variables.

6.1 Performance of Children Born Very Preterm and Full Term on the WPPSI-R at Age 6 Years

Table 6.1 shows the mean scores and achievement groups of children born very preterm and full term on the WPPSI-R measure of general cognitive ability administered at age 6 years. As described in this table, children born very preterm showed clear discrepancies in performance across all four of the subtests administered, with children born very preterm performing 12 points lower, on average, than their full term peers. Of interest, there were some differences in the effect sizes for the four subtests administered. Specifically, the effect sizes for the Picture Completion (d=0.44) and Comprehension (d=0.42) subtests were small to moderate, according to Cohen’s criteria (Cohen, 1992). In contrast, the effect size for the Arithmetic subtest (d=0.61) was relatively larger, while that for the Block Design subtest was large (d=1.00), indicating a difference of approximately 1 standard deviation in the performances of children born very preterm and full term on this measure. Thus, as a group, children born very preterm showed lower general cognitive ability, with some indication that task performance may be more impaired on subtests requiring more fluid processing skills as opposed to crystallised, learned skills.

While these results indicated clear discrepancies in performance across the two study groups, there was a possibility that children in the very preterm group achieved lower average scores due to the influence of a few children with more severe impairments. This issue was addressed by dividing children into groups according to their average performance score on the WPPSI measure. Performance groups were computed relative to the standardised mean (M=100). Table 6.1 shows the percentages of children whose performance scores from the WPPSI fell into the severely impaired (>2SD below the mean), mildly impaired (1-2 SD below the mean), average (within 1 SD) and above average (>1SD above the mean) ranges. As can be seen from this table, a large proportion (73%) of children in the very preterm group performed in the average range on this measure. However, children born very preterm were at greater risk of mild or severe impairment and were less likely to fall into the accelerated range ($p<0.001$). An examination of the groups' distributions on the IQ measure, illustrated in Figure 6.1, also indicated that the entire distribution for the very preterm group was shifted so that its peak was lower than that of the full term group. These findings suggest that the lower mean cognitive performance score in this group was not the result of extremely low performance in a select group of children with more severe difficulties, but arose due to a general group tendency toward poorer performance on this measure.

Table 6.1: Performance of Children Born Very Preterm and Full Term on the Wechsler Preschool and Primary Scale of Intelligence at Age 6 Years

	Group				
	Preterm (n=102)[a]	Full term (n=108)	t	p	*d*
Scale					
M (SD) Picture completion	10.40 (3.23)	11.66 (2.44)	3.36	0.002	0.44
M (SD) Block design	8.21 (2.81)	10.96 (2.71)	7.32	<0.001	1.00
M (SD) Comprehension	9.69 (3.06)	10.96 (2.95)	3.23	0.002	0.42
M (SD) Arithmetic	8.95 (3.20)	10.77 (3.01)	4.38	<0.001	0.59
M (SD) Total IQ score	95.46 (14.63)	106.92 (11.71)	6.35	<0.001	0.87
% Significant impairment	5	0.9			
% Mild impairment	14.9	2.8			
% Average performance	73.3	69.4			
% Above average performance	6.9	26.9	23.91	<0.001	

[a] *df* =207 and 3. 1 child refused to complete tests, 1 child did not complete Block Design or Picture Completion due to severe visual impairment
d: Cohen's *d* effect size for the difference in group means

Another possibility was that these performance discrepancies were brought about because of confounding socioeconomic selection factors. Specifically, the differences in social capital available to groups of children born very preterm and full term may have led to depressed mean scores in the very preterm group. To examine this issue, between group comparisons were replicated via ANCOVA with family SES included as a covariate. Between group differences in Picture Completion, $F(1)=6.69$, $p<0.01$; Block design, $F(1)=46.51$, $p<0.001$; Comprehension, $F(1)=8.98$, $p<0.01$; and

Arithmetic, F(1)=14.00, p<0.001 remained significant, suggesting that group differences could not be explained by SES.

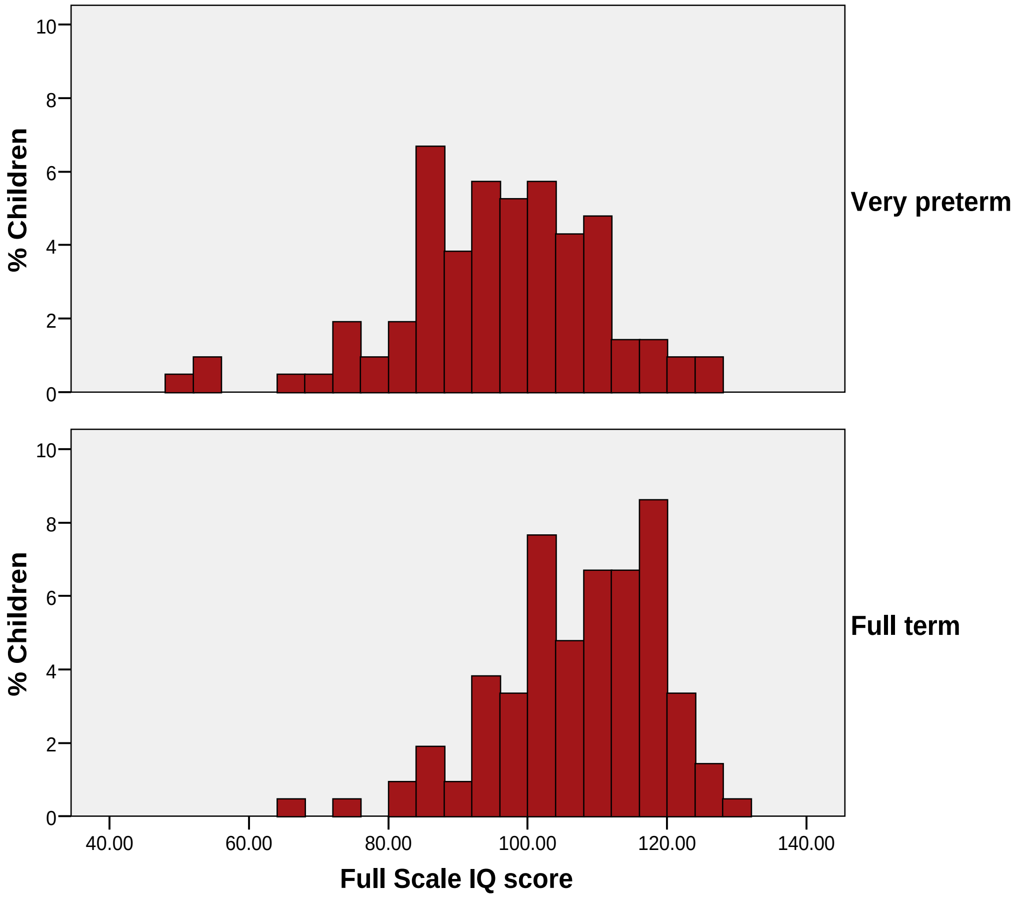


Figure 6.1: Distributions of WPPSI-R IQ Scores at Age 6 Years for Children Born Very Preterm and Full Term

6.2 Performance of Children Born Very Preterm and Full Term on Measures of Academic Achievement at Age 6 Years

Table 6.2 shows the mean performance of groups of children born very preterm and full term on three subscales of the *Woodcock-Johnson III Tests of Achievement* (Woodcock & Mather, 1989), as well as percentages of children who were rated by teachers as showing delayed or below average performance in key curricular areas. Children were excluded from the analysis of standard scores if they could not complete any items on a particular subtest.

Results showed that children in the very preterm group achieved statistically lower standardised scores for the Maths Fluency subtest ($p<0.001$). It must be noted that a number of children in the very preterm group (19.8% compared with 4.6% in the full term group) were unable to complete any mathematics problems. Despite the loss of data for this analysis, the effect size for the difference in standard scores for the Maths Fluency subtest was moderate ($d=0.68$), indicating a group tendency toward lower performance in this academic domain even when children who could not complete any of the problems were excluded.

In terms of the Understanding Directions subtest, 3 children in the very preterm group and 1 in the full term group declined to complete this test. Children in the very preterm group showed lower performance scores for Understanding Directions ($p<0.05$), with the effect size being moderate ($d=0.43$) and therefore indicating that the full term group were more likely to understand and respond to more complex sequences of instructions.

Analysis of scores for the Passage Comprehension subtest showed a tendency for those in the very preterm group to achieve lower scores on this measure ($p<0.1$), although this difference did not quite reach significance and the effect size for this group difference was small ($d=0.24$). Three children in the very preterm group were unable to complete any items on this test.

To examine whether these group differences in performance were the result of very poor performance in a small subset of children with more severe impairments, children who had been diagnosed with moderate-severe cerebral palsy at age 2 years and/or whose scores on the standardised measure were below 70 were excluded from analyses. After the exclusion of these children, there were no significant group differences in performance scores for the Passage Comprehension subtest, $t(195)=1.23$, $p=0.22$. Group differences on the Maths Fluency subtest scores remained significant, $t(178)=4.56$, $p<0.001$. For the Understanding Directions subtest, there were significant group differences in the complexity of items able to be responded to, with the very preterm group showing lower performance on this measure, $t(192)=2.60$, $p=0.01$. Thus, group differences in receptive language and mathematics achievement were not the result of low scores in a few, significantly impaired children. These standardised achievement measures therefore suggest early difficulties in key academic domains amongst children born very preterm, with impairment being greatest in the area of mathematics.

In comparison to the full term group, teachers were more likely to report that children in the very preterm group were delayed or below average in reading ($p<0.01$), mathematics ($p<0.001$) and language comprehension ($p<0.05$). These results are further illustrated in Figure 6.2. When children with moderate-severe motor impairments and/or low cognitive scores were excluded from the analysis of teacher ratings, group discrepancies in reading, $\chi^2(2)= 9.36$, $p<0.05$; mathematics, $\chi^2(2) = 21.32$, $p<0.001$; and language comprehension, $\chi^2(2) = 8.85$, $p<0.05$) persisted.

Table 6.2: Performance of Children Born Very Preterm and Full Term on Measures of Academic Achievement at Age 6 Years

	Group				
	Very Preterm (n=102)	Full term (n=108)	t/$\bullet^{2}$*	p	Effect size (*d*/OR)
% Did not complete Passage Comprehension subtest	0.5	0	1.06	0.30	0.48
Mean (SD) Passage Comprehension score	109.39 (15.33)	113 (15.50)	1.68	0.09	0.24
% Teacher rating of reading delayed/ below average	50.0	24.8	13.73	<.001	1.78
% Did not complete Maths Fluency subtest	20.6	3.7	14.26	<0.001	2.91
M (SD) Maths Fluency score	98.25 (6.35)	103.13 (7.74)	4.57	<0.001	0.68
% Teacher rating of arithmetic delayed/ below average	44.8	13.5	24.05	<0.001	2.56
% Did not complete Understanding Directions subtest	2.9	0.9	1.14	0.29	2.08
M (SD) Understanding Directions score	109.85 (15.29)	113.48 (15.50)	3.06	<0.01	0.43
% Teacher rating of comprehension delayed/below average	31.3	14.3	8.31	0.004	1.73

df=174-204 for standardised tests; *df*=1 for teacher ratings; OR: Odds ratio

Examination of the extent to which group differences in academic achievement were the result of confounding socio-economic discrepancies between the two study groups showed that the group differences in scores for the Maths Fluency, $F(1)=16.05$, $p<0.001$; and Understanding Directions subtest scores, $F(1)=4.61$, $p<0.05$ remained statistically significant after covariate adjustment for SES. SES was also significantly related to children's scores on the Understanding Directions measure, $F(1)=11.30$, $p<0.01$. After covariate adjustment for SES, group differences for teacher ratings of reading performance ($p<0.01$), mathematics ($p<0.001$) and language comprehension ($p<0.05$) persisted. SES was also significantly associated with mathematics achievement ($p<0.05$). These findings suggest that group differences in academic achievement were unlikely to be the result of differences in SES.

Together, findings from standardised tests administered at age 6 are consistent with international studies suggesting that children born very preterm achieve lower mean cognitive performance scores and have higher rates of mild and severe cognitive delay. Furthermore, findings for both standardised achievement tests conducted in the laboratory and teacher ratings of performance in a classroom environment were consistent in showing that children born very preterm were more likely to have difficulty in reading, mathematics and language comprehension. However, it appears that in terms of reading these differences may have arisen due to the poorer reading performance of children with more general cognitive and/or motor delays. The most pronounced group differences were in mathematics achievement. Even when children with significant motor impairment or cognitive delay were excluded from analysis, children in the very preterm group were more likely to achieve lower scores on the Woodcock-Johnson test of Maths Fluency and were more likely to be rated by teachers as performing below average in mathematics.

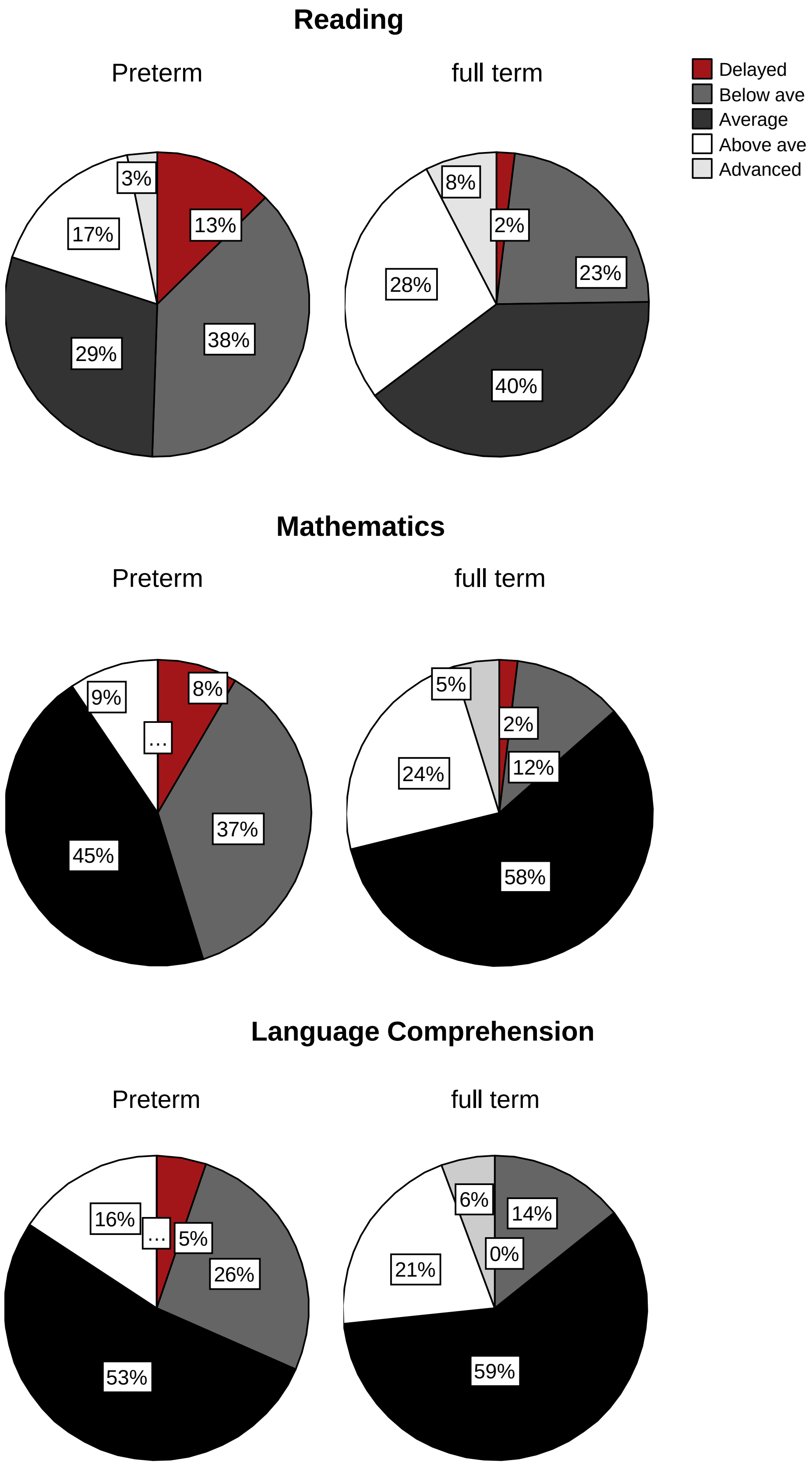


Figure 6.2: Teacher Ratings of the Academic Performance of Children Born Very Preterm and Full Term

While these findings offer a global description of the outcomes of children born very preterm at early school age, they do not allow for an understanding of the process mechanisms contributing to these outcomes. Indeed, these more general findings raise important questions as to the specific cognitive deficits that may make it difficult for these children to perform in a classroom environment. It is probable that difficulties in specific executive areas such as attentional flexibility, working memory, inhibitory control, planning and self-monitoring play an important contributing role in the academic performance of these children. These executive functions form the focus of the following chapter.

Chapter 7

Results 2: Executive Function Performance at Age 6 Years in Children born Very Preterm and Full Term

The first aim of this study was to describe the executive function performance of a group of children born very preterm in relation to their full term peers at early school age. To address this aim, this chapter presents a series of analyses comparing the performance of children born very preterm and children born full term on eight measures of executive function. These measures, administered at age 6 years (adjusted for gestational age at birth), included six laboratory-based measures of short term and working memory (Digit Span and Corsi blocks), planning and problem solving (Tower of Hanoi), inhibitory control and cognitive flexibility (Detour Reaching Box), sustained attention and inhibition (K-CPT) and selective attention (NEPSY Visual Search). In addition, parents and teachers completed the BRIEF and behavioural ratings were completed by examiners following each child's neuropsychological assessment. A second and related aim addressed in this chapter was to examine the extent to which impairments in the very preterm group arose due to more severe global impairments in a small subset of children born very preterm, as opposed to being more generally apparent across this study group. Third, it was important to clarify whether differences in executive function were attributable to group differences in socio-economic circumstances. This issue is addressed in the final part of the chapter.

Between group differences on each of the measures of executive function were examined in three steps. First, all data was visually inspected, using scatterplots and box plots, to determine if data distributions were uniform. In addition, Kolmogorov-

Smirnoff Tests were used to check the assumptions for data distribution normality. These analyses showed that, across all measures, data did not meet the assumptions for a normal distribution. Instead, data distributions for both the very preterm and full term groups were positively skewed for measures of working memory (Digit span and Corsi blocks) and the Tower of Hanoi and negatively skewed for the Detour Reaching Box, Visual Search, BRIEF and behavioural ratings. The exception was in the case of the K-CPT, where the data of the full term group was negatively skewed for the measure of sustained attention (omission errors), while the very preterm group showed a more flattened distribution. Levene's tests for homogeneity of variances showed that, for a number of measures, variances in scores for each group were significantly different.

Second, the performance of all children born very preterm and children born full term was compared on the eight measures of executive function. For consistency and ease of reporting, the results of independent samples t-tests are reported for continuous data and Chi-Squared tests of independence are reported for categorical data. However, all continuous data was reanalysed using the non-parametric Mann-Whitney U-test for independence, with any discrepancies between parametric and non-parametric test findings reported in text. Where applicable, the results of t-tests are reported after correction for non-homogeneous variance.

Third, analyses were repeated excluding children with moderate to severe neurodevelopmental impairment, defined as a WPPSI IQ score greater than 2 standard deviations below the standardised mean (i.e. <70) or a clinical diagnosis of moderate to severe cerebral palsy. Finally, children were allocated to achievement groups based in order to more succinctly describe their performance on each laboratory-based measure of executive function and to permit comparisons across measures. These achievement rankings (1-4) were determined through visual inspection of data for natural cut points.

7.1 Performance of Children Born Very Preterm and Full Term on Measures of Verbal and Spatial Short Term/Working Memory

Table 7.1 describes the performance of children born very preterm and children born full term on the Digit Span and Corsi Blocks tasks. The Digit Span task assesses verbal short term and working memory, while the Corsi Blocks task assesses spatial short term and working memory. Two measures of a child's performance on each task were obtained for 1) trials where required recall was in forwards sequence and 2) trials where recall was in backwards sequence. First, a raw score, comprising the number of trials the child was able to pass, is recorded. Second, a span score, indicating the highest number of digits/ blocks they were able to recall in sequence, is reported.

As shown in Table 7.1, during the forward phase of the Digit Span task, there was a tendency for children in the very preterm group to complete fewer trials correctly ($p=0.11$) and to recall fewer digits in sequence than their full term peers ($p=0.13$). However, group differences were not significant. Across both groups, children experienced greater difficulty during the second, backward phase of the task, with a number of children failing to understand task requirements even after repeated instruction. This difficulty was particularly marked amongst children born very preterm, with 13%, compared to 4% of the children in the full term group, being unable to pass the required two criterion trials after repeated explanation ($p<0.05$). As a consequence, fewer children in the very preterm group (n=90) proceeded to the backward digit span trials. This is illustrated in Figure 7.1a.

An examination of between group differences for children who were able to complete the backwards Digit Span phase showed that children born preterm passed fewer backward trials, although this was at a trend level of significance (p=0.06). No significant between group differences were found on the measure of the highest span of digits children achieved (p=0.57) suggesting that children in the very preterm group were able to achieve the same backward memory span level as those in the full term group even though they passed fewer trials. However, it is important to note that there was some evidence of a floor effect for the backward Digit Span measure, since children were generally only able to repeat back 2 or 3 digits in the correct order. Analysis of all results for the Digit Span task using Mann-Whitney U-tests demonstrated a consistent pattern of findings. Taken together, these results suggest that children in the very preterm group had more difficulty than their full term peers in remembering and repeating back sequences of verbal information when working memory demand was high and children were required to repeat back numbers in reverse order.

Table 7.1 also shows that during the first, forward phase of the Corsi Blocks task, children born very preterm did not differ from those born full term in the number of trials they were able to pass (p=0.29) or the length of span they were able to recall (p=0.64), suggesting that children born very preterm were as likely as those born full term to remember sequences of spatial information in forward sequence. As had been the case for the Digit Span backwards task, a number of children were unable to understand the ‘backwards’ requirement for this task after several demonstrations. Thus, 16% of children in the very preterm and 8% of children in the full term group did not pass the four criterion trials for this task and were unable to proceed to any backwards sequence trials ($p=0.10$). Even with this reduction in the number of very preterm children included in the between group analysis of this phase ($n=86$), the remaining children in the very preterm group obtained significantly lower scores on the backwards sequence trials than those in the full term group. Children born very preterm passed fewer trials ($p<0.01$) and achieved lower span levels ($p<0.001$) than children born full term. Categorical analyses of the move levels passed showed that children in the very preterm group were less likely to achieve higher span levels, with only 7% achieving a backward span level greater than three compared to 24% of children in the full term group ($p<0.01$). Figure 7.1b shows that as the task increased in difficulty, fewer children in the very preterm were able to repeat block sequences correctly.

Table 7.1: Performance of Children Born Very Preterm and Full Term on Measures of Short Term/Working Memory

	Group				
	Preterm (n=102)	Full term (n=108)	t/χ^2	p	*d*/OR
M (SD) Raw score Digit Span forwards	5.88 (1.36)	6.19 (1.46)	1.60	0.11	0.22
M (SD) Forward Digit Span	4.22 (0.75)	4.39 (0.82)	1.53	0.13	0.22
% Passed criterion trials for digit span backwards	87.4	96.3	5.66	0.02	1.65 (1.21-2.23)
M (SD) Raw score Digit Span backwards	4.57 (1.36)	4.91 (1.15)	1.90	0.06	0.27
M (SD) backward Digit Span	2.69 (0.59)	2.74 (0.59)	0.57	0.57	0.09
M (SD) Raw score Corsi Blocks forward	5.42 (1.66)	5.67 (1.69)	1.07	0.29	0.19
M (SD) Forward Corsi Blocks span	3.26 (0.94)	3.32 (0.92)	.47	0.64	0.05
% Passed criterion trials for Corsi Blocks backward	84.3	91.7	2.70	0.10	1.38 (1.00-1.92)
M (SD) Raw score Corsi Blocks backward	2.63 (1.16)	3.25 (1.30)	3.42	0.001	0.50
M (SD) backward Corsi Blocks span	2.59 (0.74)	2.93 (0.86)	2.83	<0.01	0.43

df=183-209 for t-tests and 1 for chi-squared measures

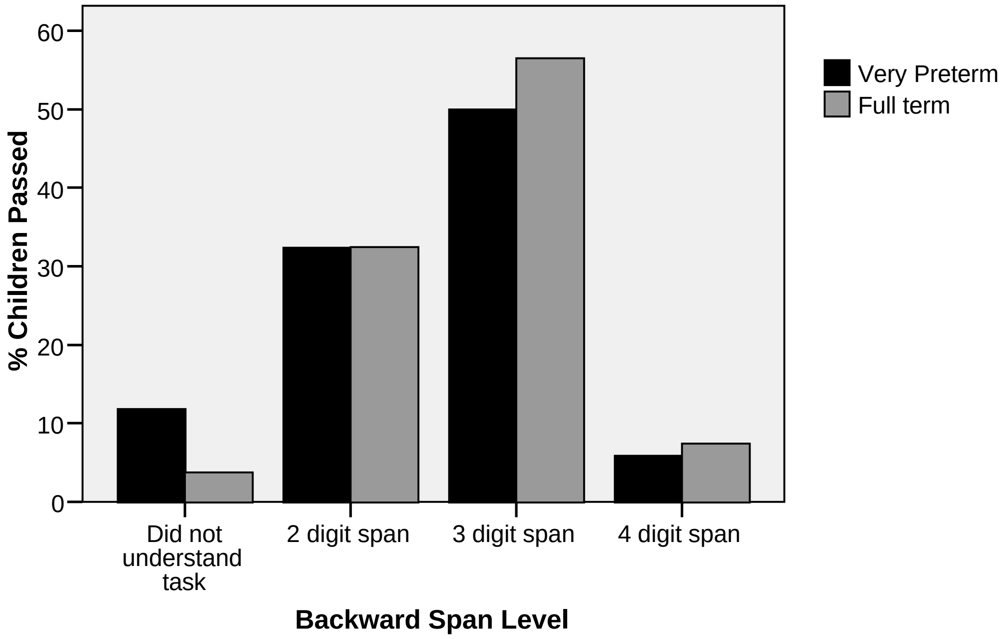


Figure 7.1a: Performance of Children Born Very Preterm and Full Term on the Backward Digit Span Task

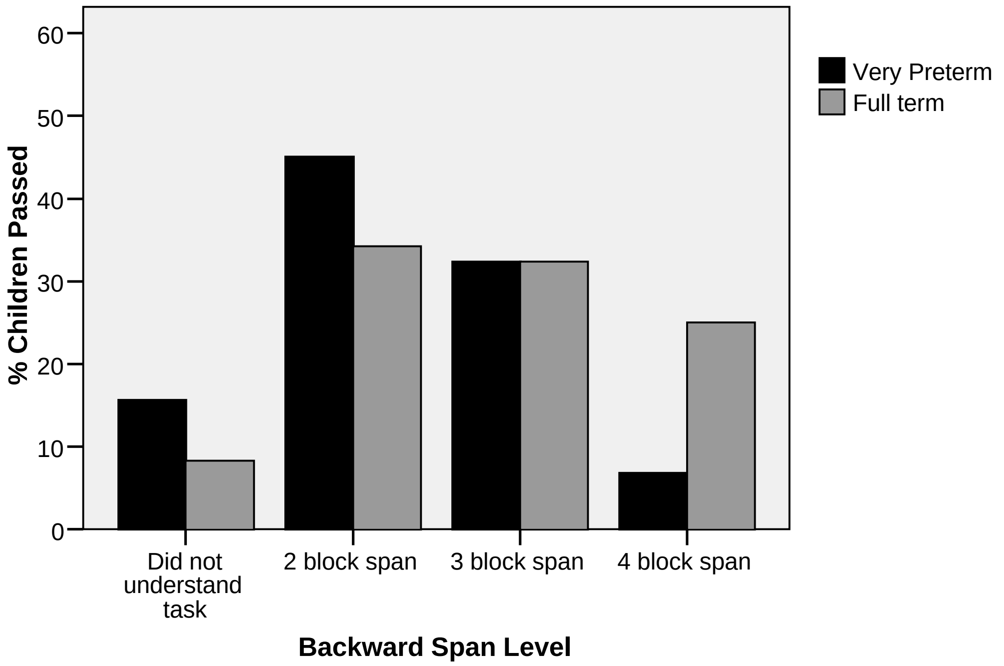


Figure 7.1b: Performance of Children Born Very Preterm and Full Term on the Backward Corsi Blocks Task

Exclusion of Scores of Children with Severe Neurodevelopmental Impairment. An examination of the extent to which group differences in performance on the working memory tasks persisted after the exclusion of children with severe intellectual and motor impairments showed that there were no significant between group differences in the number of digits able to be recalled in forwards sequence for either task. The effect size for the group difference in the number of digits able to recalled in backwards sequence was reduced ($d=0.23$, $p=0.10$). However, group differences in the spatial block sequences able to be recalled in backwards sequence remained significant ($p<0.05$), suggesting that the differences in performance across the two groups could not be attributed to extremely low performance amongst this subset of children.

Summary Scores for Working Memory Measures. Based on their performance on the measures of backward digit and spatial span, children were divided into one of 4 groups for each measure. These groups were the same as those shown in Figure 7.1a and 7.1b.

7.2 Performance of Children Born Very Preterm and Full Term on the Tower of Hanoi

Table 7.2 describes the performance of children born very preterm and full term on the Tower of Hanoi planning/problem solving task. This analysis excludes two children in the very preterm group who declined to complete the task. All other children were able to articulate the rules for the Tower of Hanoi and were assigned a score for the task. Analysis of the total scores for the task showed that children in the very preterm group achieved lower scores than their full term peers ($p<0.01$). Examination of the reasons for failure/discontinuation of this task showed that children in the very preterm group were more likely to fail the task because they made two consecutive rule breaks at one move level ($p<0.05$), as opposed to failing because they completed the task in a greater number of moves than required. This suggests that children in the full term group were more likely to try to complete the task while abiding by the rules, while those in the very preterm group tended to respond more impulsively.

As a further illustration of group differences on this task, the proportion of children passing and thereafter discontinuing at each move level of the Tower of Hanoi is shown in Figure 7.2. As shown, a smaller proportion of children in the very preterm group passed the initial 2-move level ($p=0.05$). Similarly, chi-squared tests comparing the percentages of children who passed various move levels indicated that children in the very preterm group were more likely to fail at lower levels, $\bullet^2= 12.64$, $p=0.05$.

Exclusion of Scores of Children with Severe Neurodevelopmental Impairment. When children with IQ scores below 70 and/or moderate to severe CP were excluded from analysis, results for the Tower of Hanoi task were consistent with those reported above. Group differences in the scores achieved and number of children failing because they broke rules on the task continued to be significant ($p<0.05$).

Table 7.2: Performance of Children Born Very Preterm and Full Term on the Tower of Hanoi Planning Task

	Group				
	Very preterm (n=100)	Full term (n=108)	t/χ^2	p	*d*/OR
M (SD) Total score	3.13 (2.04)	3.85 (2.10)	2.51	0.01	0.35
% Task ceased due to consecutive rule breaks	77.7	54.7	11.61	0.001	1.83 (1.24-2.70)

df=207

Summary Measure for Performance on the Tower of Hanoi. Based on their performance on the Tower of Hanoi task, children were divided into groups. Those children who did not pass both of the 2-move level trials for the task were allocated a score of 1, indicating that they were able to articulate, but could not abide by the rules. Children who were able to pass the 2-move level, indicating that they could effectively abide by the rules, were allocated a score of 2. Children who were able to pass the 3-move trials, suggesting that they were able to plan ahead and inhibit the tendency to place the smaller disk on the incorrect goal post were allocated a score of 3. Finally, children who succeeded in correctly completing higher levels of the task, suggesting a more advanced ability to plan ahead, generate a strategy and overcome goals, were allocated a score of 4.

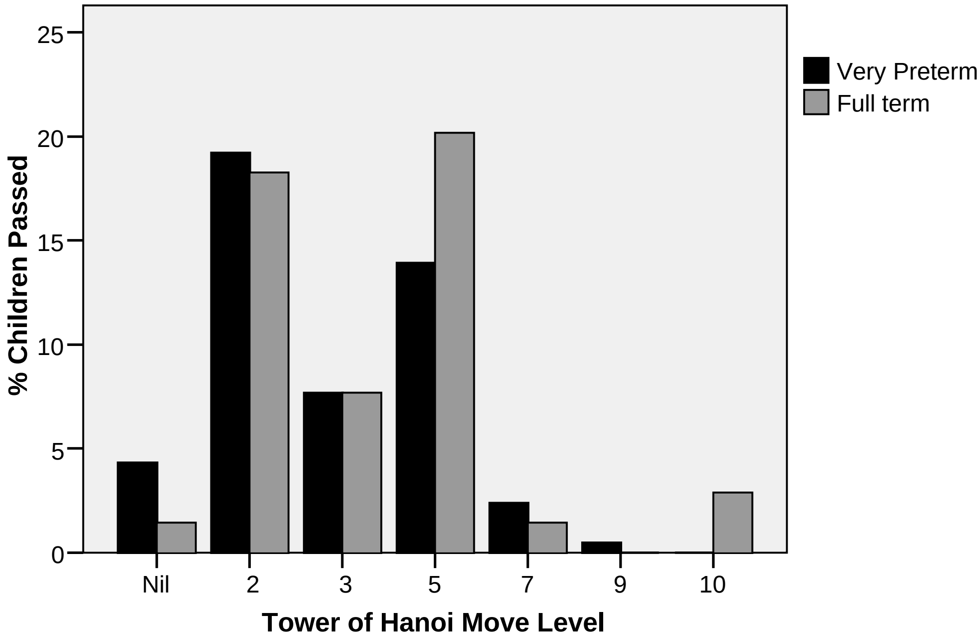


Figure 7.2: Performance of Children Born Very Preterm and Full Term on the Tower of Hanoi

7.3 Performance of Children born Very Preterm and Full Term on the Visual Search Task

Table 7.3 describes the performance of children born very preterm and full term on the Visual Search measure of selective attention. As part of this task, two search trials (cats and faces) were administered, with the mean number of correct responses, incorrect responses and time taken to complete searching computed for each trail. These scores are used to create an overall accuracy score (correct - incorrect responses), a summed duration of search measure and a search efficiency score (Korkman, 1990). The results of 7 children in the very preterm and 3 children in the full term group were excluded from analysis because they crossed out all items on the page, indicating that they had a poor understanding of task instructions.

Results showed that children in the very preterm group correctly identified fewer target items on the first (cats) trial of the task ($p<0.05$). They also made more errors of commission on this trial by selecting more stimuli that were not targets ($p=0.05$). While the full term group spent a longer time searching for items, this difference did not reach significance ($p=0.21$).

Similarly, across the second (boy/girl faces) phase of the task, children in the very preterm group correctly identified fewer target items than their full term peers ($p=0.06$) and selected more incorrect non-target items from the array of pictures ($p<0.04$). During this trial, there was also a tendency for children in the full term group to take longer to search for items ($p=0.07$).

Overall, children in the very preterm group were lower in terms of their accuracy (i.e. they made more errors of omission) on the Visual Search task ($p<0.01$). However, the full term group took longer to complete the searches ($p=0.05$). Therefore, no significant differences in overall efficiency were found between the groups. Similar results were obtained using non-parametric tests.

Table 7.3: Performance of Children Born Very Preterm and Full Term on the Visual Search Task

	Group				
	Preterm (n=102)	Full term (n=108)	t/χ^2	p	*d*/OR
% Unable to understand task requirements	6.9	3.7	1.06	0.30	1.33 (0.83-2.13)
Trail 1: Cats					
M (SD) Correct responses	17.63 (2.94)	18.63 (2.33)	2.68	0.01	0.38
M (SD) Non-target errors	0.48 (2.10)	0.07 (0.25)	2.01	0.05	0.28
M (SD) Time	59.01 (26.44)	63.65 (27.38)	1.20	0.21	0.18
Trial 2: Faces					
M (SD) Correct responses	10.98 (5.06)	12.31 (4.74)	1.99	0.05	0.27
M (SD) Non-target errors	7.49 (8.87)	5.35 (6.71)	1.64	0.10	0.28
M (SD) Time	132.76 (52.24)	144.85 (45.18)	1.85	0.07	0.26
Overall Performance					
M (SD) Total accuracy	20.63 (10.49)	25.58 (8.29)	3.71	<.001	0.53
M (SD) Total time	190.98 (65.73)	208.93 (55.94)	2.08	0.04	0.28
M (SD) NEPSY score	10.46 (2.81)	10.94 (2.60)	1.25	0.21	0.20

Note. df=197

Exclusion of Scores of Children with Severe Neurodevelopmental Impairment. When children with more severe neurodevelopmental impairments were excluded from the above analyses of the Visual Search results, there was a significant group difference in terms of accuracy, with children in the very preterm group obtaining lower accuracy scores than their full term peers ($p<0.05$). Unlike the results reported above, children in the very preterm and full term groups did not differ in the time spent searching, $t(189)=1.50$, $p=0.14$. Thus, in general, children in the very preterm group correctly identified fewer items on this task and made more errors of commission, leading to lower accuracy in searching.

Summary Scores for Visual Search Task. Summary scores for the Visual Search task were based on accuracy scores, as this was the principle measure on which groups had differed in performance. In order to compose summary scores for this task, the distribution of the full term group was visually inspected for evident cut points. Group distributions of continuous scores are shown in Figure 7.3. All children whose errors on the visual search had exceeded their correct responses were assigned the lowest rating of 1 for their performance. Children in both the preterm (n=7) and full term (n=3) group who had selected all stimuli during the second search phase were also assigned this score. Given that an accuracy score below 20 appeared to reflect the tail end of the distribution of the full term group, children whose scores were below 20 were allocated a score of 2. Children who achieved scores between 30 and 40 were allocated a score of 3, while those at the top end of the control distribution (>30) were assigned a score of 4.

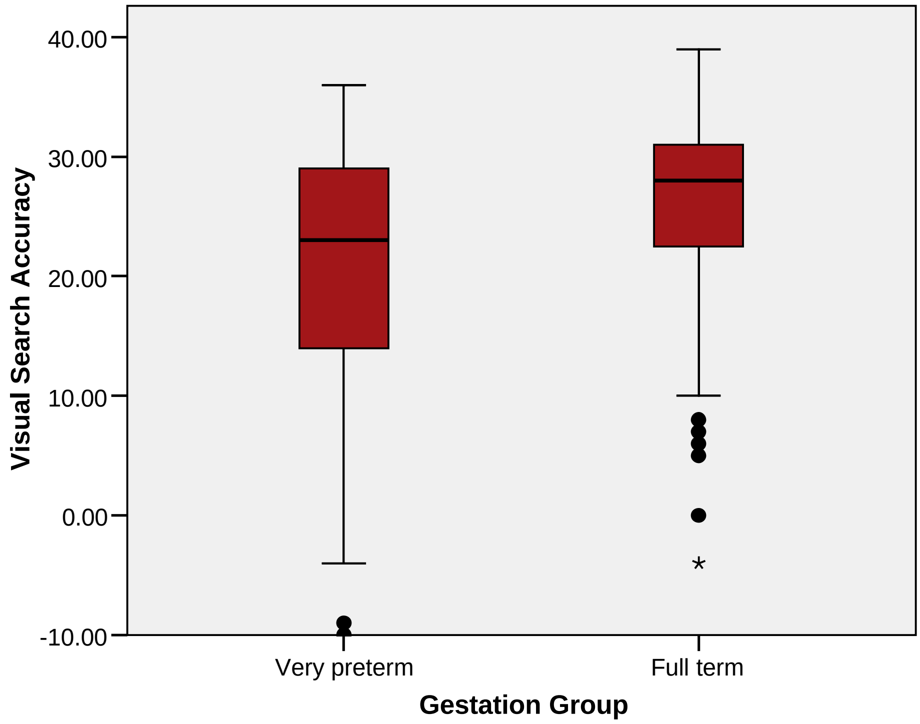


Figure 7.3: Mean Visual Search Accuracy of Children born Very Preterm and Full Term

7.4 Performance of Children Born Very Preterm and Full Term on the Detour Reaching Box

Table 7.4 describes the performance of groups of children born very preterm and full term on the Detour Reaching Box task. This task assessed children's ability to learn three strategies over progressive phases of the task (phase 1 – direct route phase, phase 2 - yellow light phase and phase 3 - green light phase) and flexibly alter their use during a final, alternating phase. During completion of each phase, the number of incorrect direct reaches and the number of incorrect switch errors (returning to a former strategy when a new one was required) were recorded. The percentage of children who made such errors is also shown as data were skewed for parametric measures. Children were required to demonstrate 3 consecutive correct responses at each task phase in order to pass and graduate to the next phase. If children did not reach this criterion within the 15 prescribed trials at each phase, the task was terminated. The number of children passing each phase is also shown in Table 7.4.

All children successfully passed the initial training phase of the task by directly reaching into the box on 3 consecutive trials. During the second, ‘yellow light’ phase of the task, 97% of children in the very preterm group and 99% of children in the full term group were able to master the strategy ($p=0.27$). However, children in the very preterm group required more training trials to achieve the criterion ($p<0.05$). Further analysis showed that 40% of children in the very preterm group committed direct reach errors during training for the first strategy and 26% of children in the full term group committed such errors ($p<0.05$).

Between group differences became increasingly apparent during the third, ‘green light’ phase of the task, with 88% of children in the very preterm group and 98% of children in the full term group correctly applying the strategy over 3 consecutive trials within the 15 prescribed trials ($p<0.001$). Further analyses showed that children in the very preterm group were more likely to revert to former strategies, with 36% of these children making direct reach errors as opposed to 12% in the full term control group ($p<0.001$) and 13% of children in the very preterm group making switch errors, as opposed to 2% of children in the full term group ($p<0.01$). However, children in the very preterm group were no more likely than those in the control group to make motor errors ($p=0.34$). Thus, children in the very preterm group were less likely to be able to learn a rule during the first training phase of the task and then were less likely to switch to a new rule despite being allowed 15 trials to do this. This meant that fewer children in the very preterm group graduated to the final phase of the task.

During the final phase of the Detour Reaching Box task, which required children to alternate flexibly between strategies, the children in the very preterm group showed a tendency to reach directly into the box more often than those in the full term group. This difference was at a trend level of significance ($p=0.06$). Performance of the groups of children born preterm and full term did not differ significantly on other measures. Collectively, results on this task showed that children in the very preterm group were more likely to reach directly into the box during all phases of the task, but that groups showed relatively similar performance during the final, alternating task phase.

Table 7.4: Performance of Children Born Very Preterm and Full Term on the Detour Reaching Box

	Group				
	Preterm (n=96)	Full term (n=107)	t/χ^2	p	OR
Phase 1: Direct route phase					
% Achieved criterion	100	100			
Phase 2: Yellow light (inhibitory control) phase					
% Achieved criterion	96.9	99.1	1.23	0.27	1.60 (0.89-2.87)
% Direct reach errors	38.9	25.5	4.19	0.04	1.37 (0.99-1.88)
Phase 3: Green light (set-shifting) phase					
% Achieved criterion	87.5	98.1	8.80	0.002	1.91 (1.47-2.50)
% Direct reach errors	13.2	1.9	9.36	0.002	3.96 (1.09-14.38)
% Motor errors	31.9	25.7	0.91	0.34	0.87 (0.64 - 1.18)
% Switch errors	35.9	12.4	15.12	<0.001	2.16 (1.34-3.48)
Phase 4: Alternating phase					
% Direct reach errors	50	36.5	3.45	0.06	1.35 (.99-1.85)
% Motor errors	28.9	24.0	0.57	0.45	0.15 (.81-1.62)
% Switch errors	66.3	60.6	0.64	0.42	1.14 (0.81-1.63)

Note. df=1

Exclusion of Scores of Children with Severe Neurodevelopmental Impairment. When children with neurodevelopmental impairments were excluded from the analysis of results for the Detour Reaching Box, findings were consistent with those reported above. Specifically, children in the very preterm group showed a tendency to make more perseverative, direct reach errors during the second, yellow light phase of the task ($p=0.06$), were more likely to make direct reach errors ($p<0.01$) and switch errors during the third, green light phase of the task ($p<0.01$) and were less likely to pass this third, green light phase ($p<0.01$). There were no group differences in performance during the third, alternating phase of the task.

Summary Scores for Detour Reaching Box. As a summary of their performance on the Detour Reaching Box, children were divided into groups, based on inspection of frequencies of error. Those children who were unable to pass the yellow or green light phases of the task were allocated a score of 1. Those who were able to pass the training trials, but made more than five errors, were allocated a score of 2. Children who made fewer than five errors across all task phases were allocated a score of 3, while those who made no direct reach or shift errors throughout completion of the task were allocated a score of 4.

7.5 Performance of Children Born Very Preterm and Full Term on the Kiddie-Continuous Performance Test (K-CPT)

Table 7.5 describes the performance of children born very preterm and full term on the K-CPT attention/inhibitory control task. Measures from this task include an indicator of sustained attention, recorded as the percentage of failures to respond when a response was required (omission errors), and a measure of inhibitory control, recorded as the percentage of responses made when responses were not required (commission errors). As some children failed to complete all 200 trials of this task and ceased responding before 7 minutes, scores were averaged across the number of trials that children completed. In addition, the number of trials children completed overall, average time to respond to stimuli, and the percentage of perseverative errors, assessed as the number of times children responded before 100ms, are presented. Numbers for each group are reduced due to technical issues with computerised data (n=8) or children's refusal to complete this task (n=7).

As shown in Table 7.5, children in the very preterm group were more likely to make errors of omission on this task ($p<0.01$). Figure 7.4 shows the pattern of these errors over the 10 blocks of the K-CPT task. During the first segment of the task, children across both groups made a higher number of omission errors. Thereafter, the number of omission errors was initially low, but increased over time. Across most of the trial blocks (including blocks 3, 4, 5, 6, 7 and 8), children in the very preterm group made more errors of omission than their full term peers ($p<0.05$). However, for blocks 9 and 10, the level of omission errors did not differ significantly between the groups.

Analysis of the mean percentage of errors of commission on the K-CPT showed that the children in full term group made more errors of commission, responding more often to non-target stimuli than children in the very preterm group ($p<0.01$). As shown in Figure 7.5, the mean number of errors of commission was significantly higher in the full term group during the middle trials (Blocks 4, 5; $p<0.001$), when children in the very preterm group were making more errors of omission. However, an analysis of the overall error rates (including both types of errors) showed that children in the very preterm group were less accurate, completing fewer trials correctly overall ($p<0.01$).

Further group comparisons showed that children in the very preterm group took longer to respond to stimuli on this task ($p<0.05$), with the pattern of slower response times being consistent across all 10 blocks of trials. There were no group differences in the percentages of perseverative errors (responses before 100ms; $p=0.18$). Analyses using non-parametric Mann-Whitney tests revealed consistent findings.

Table 7.5: Performance of Children Born Very Preterm and Full Term on the Kiddie's Continuous Performance Task

	Group				
	Very preterm (n=95)	Full term (n=100)	t	p	*d*
M (SD) Number of trials completed	188.84 (29.13)	195.60 (16.96)	1.99	0.05	0.29
M (SD) % Omission errors over required response trials	21.19 (16.06)	13.28 (11.51)	3.97	<0.001	0.59
M (SD) % Commission errors over commission trials	36.60 (16.76)	44.34 (17.28)	3.13	0.002	0.53
M (SD)% Incorrect responses overall	25.05 (12.23)	21.05 (9.01)	2.61	0.01	0.38
M (SD) Time to respond	622.79 (121.82)	589.24 (107.81)	2.04	0.04	0.29
M (SD) % Perseverative errors	2.78 (3.59)	2.22 (3.06)	1.17	0.24	0.17

Note. df=150-193

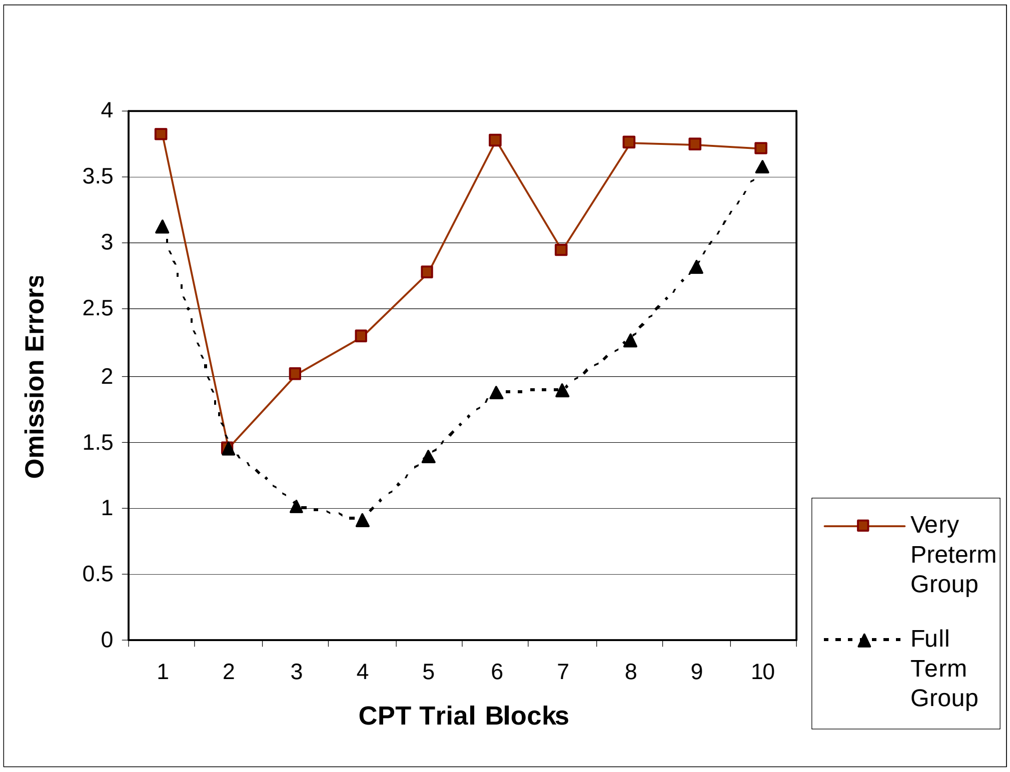


Figure 7.4: Mean Number of Omission Errors of Children Born Very Preterm and Full Term Over 10 Trial Blocks of the K-CPT

Exclusion of Scores of Children with Severe Neurodevelopmental Impairment. An analysis of the K-CPT task scores including only the scores of children without significant neurodevelopmental impairments showed a pattern of results that was consistent with those reported above. Children in the very preterm group made more errors of omission ($p<0.001$), fewer errors of commission ($p<0.01$) and more errors overall ($p<0.05$). They also took longer to respond to stimuli than their full term peers ($p<0.05$).

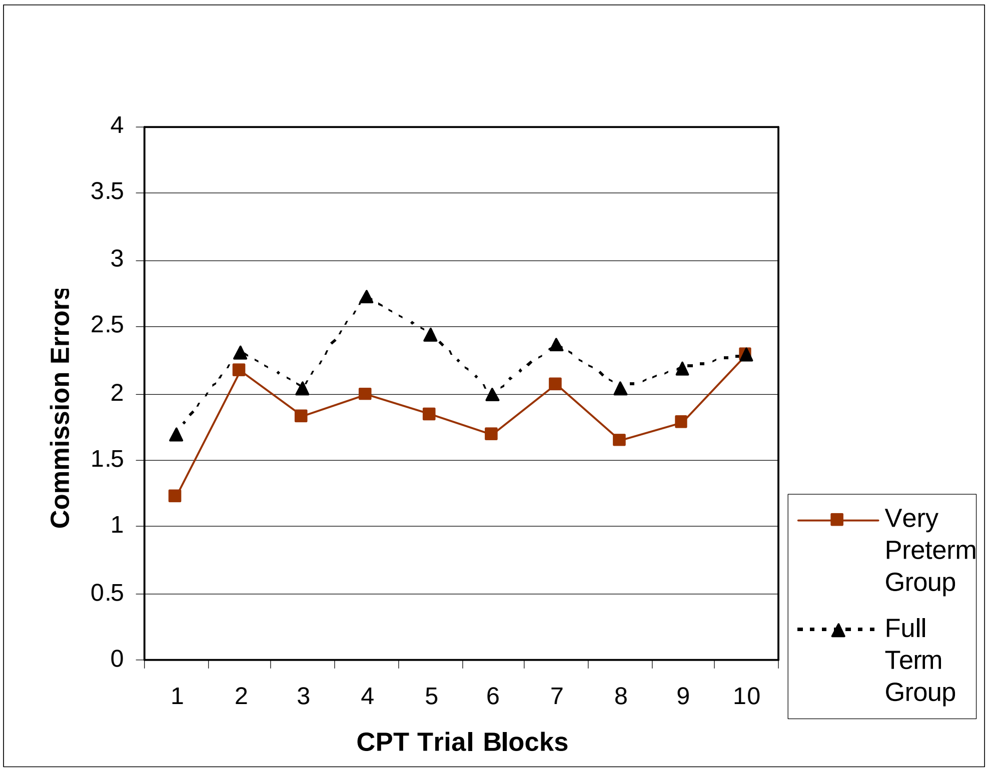


Figure 7.5: Mean Number of Commission Errors of Children Born Very Preterm and Full Term Over 10 Trial Blocks of the K-CPT

Summary Scores for Continuous Performance Task. Given that the primary K-CPT measure on which children born very preterm had shown difficulties relative to those born full term was for level of errors of omission, this score was used to summarise performance on this task. The percent of omission errors over the omission trials only was considered so as to separate out this component of the task from the inhibitory control component. In order to create summary scores, the distribution of scores for the full term group was inspected visually. It was clear that most of the distribution of scores in the full term group was centred around a peak of 10%, with a standard deviation of approximately 10% either side of the mean. This distribution was very different to that of the preterm group, which was flatter with greater variance. Based on the full term group distribution, children who made omission errors on more than 40% of omission trials were allocated a summary score of 1. Children who made errors for more than 10% of trials, but less than 20%, were assigned a score of 2. Those who made errors on 20-40% of the trials were allocated a score of 3. Finally, children who made omission errors on fewer than 10% of trials were assigned a score of 4.

7.6 Performance of Children Born Very Preterm and Full Term on Parent and Teacher Versions of the Behavioural Rating Inventory of Executive Function

Table 7.6 shows the mean scores for each subscale of the BRIEF parent (black ink) and teacher (blue ink) report measures, including composite scores of Metacognition and Behavioural Regulation. Children in the very preterm group were rated by their parents as having greater difficulties across all subscales apart from the Organisation of Materials scale ($p=0.67$). Scales on which groups differed therefore included: Inhibitory control ($p<0.05$), Shift ($p<0.001$), Emotional control ($p<0.01$), Initiation ($p<0.001$), Working memory ($p<0.01$), Planning ($p<0.001$) and Monitoring ($p<0.001$). In addition, children in the very preterm group were rated as having more difficulty in utilising metacognitive skills overall ($p<0.001$) and as having more difficulties in regulating their emotions and behaviour ($p<0.001$). Subsequent analysis using non-parametric tests yielded consistent findings.

Children in the very preterm group were rated by their teachers as having greater difficulties across all subscales apart from the Emotional Regulation subscale ($p=0.11$). Scales on which groups differed therefore included: Inhibitory control ($p<0.05$), Shift ($p<0.01$), Initiation ($p<0.01$), Working memory ($p<0.01$), Planning ($p<0.01$), Organising Materials ($p<0.05$) and Monitoring ($p<0.05$). Across the composite scales of Behavioural Regulation and Metacognition, teachers of children born very preterm were more likely to report difficulties than those of children born full term ($p<0.05$). Non-parametric analyses revealed consistent findings.

In terms of the clinical significance of these findings, guidelines for the BRIEF specify that a t-score above 65 (or 1.5 SDs above the mean of the validation sample) should be considered abnormally high. For the parent reported BRIEF ratings, only 15% of children in the very preterm group obtained scores exceeding this clinical cut-off for the emergent metacognition index. Nonetheless this was significantly greater than the number of children in the full term group (5.6%) who obtained clinically significant scores ($p<0.05$). Thus, children in the preterm group were twice as likely to show clinically significant difficulties in metacognition. Similarly, for the behavioural regulation index, 14% of children in the very preterm group obtained scores that exceeded this clinical threshold, while only 4% of those in the full term group were rated as having such high scores ($p<0.01$). Thus, children in the preterm group were over three times more likely to be reported by parents as having clinically significant difficulties in regulating their emotions and behaviour.

Despite the fact that teachers rated children in the very preterm group as having elevated levels of executive difficulty, children in the full term group were as likely to meet clinical cut off criteria for difficulties in these domains. Specifically, 15% of children in the very preterm group and 10% of children in the full term group were rated by teachers as being above the clinical threshold for difficulties with metacognition ($p=0.27$). Teachers rated 16% of children in the very preterm and 13% of children in the full term group as being above the clinical threshold for difficulties with behavioural regulation ($p=0.64$).

Exclusion of Scores of Children with Severe Neurodevelopmental Impairment. When children with severe cerebral palsy or cognitive scores at least two standard deviations below 100 were excluded from the analysis of parent and teacher BRIEF ratings, group discrepancies remained consistent with those for the full sample.

Table 7.6: Parent and Teacher-Reported Executive Behaviour of Children Born Very Preterm and Full Term on the Behaviour Rating Inventory of Executive Function

	Group				
	Preterm (n=102)	Full term (n=108)	t/χ^2	p	*d*
M (SD) BRIEF inhibitory control	53.40 (9.17) 53.53 (10.42)	50.34 (8.65) 50.29 (8.67)	2.47 2.40	0.01 0.02	0.35 0.34
M (SD) BRIEF shift	52.90 (13.17) 56.49 (10.83)	47.53 (9.52) 52.14 (9.24)	3.48 3.05	0.001 0.003	0.47 0.44
M (SD) BRIEF emotional control	52.16 (11.77) 56.39 (11.74)	48.61 (10.32) 53.87 (10.51)	2.30 1.60	0.02 0.11	0.32 0.20
M (SD) BRIEF initiation	49.42 (10.64) 56.45 (10.20)	44.63 (9.01) 51.53 (9.02)	3.51 3.62	0.001 <0.001	0.49 0.51
M (SD) BRIEF working memory	52.73 (13.45) 59.04 (13.36)	47.57 (10.76) 53.14 (12.93)	3.06 3.09	0.003 0.002	0.38 0.45
M (SD) BRIEF planning	54.09 (11.20) 57.06 (12.43)	47.85 (8.45) 51.94 (10.60)	4.52 3.12	<0.001 0.002	0.63 0.45
M (SD) BRIEF organisation of materials	52.60 (11.90) 55.55 (10.52)	53.37 (2.75) 52.54 (8.38)	-.48 2.28	0.63 0.05	0.07 0.32
M (SD) BRIEF monitoring	49.49 (11.64) 54.90 (11.56)	42.93 (11.35) 51.04 (10.57)	4.34 2.19	<0.001 0.03	0.61 0.35
M (SD) BRIEF behavioural regulation index	52.26 (11.80) 54.89 (12.20)	47.82 (9.45) 51.17 (11.63)	3.00 2.21	0.003 0.03	0.42 0.31
M (SD) BRIEF metacognition index	51.93 (12.06) 50.94 (13.57)	46.46 (9.81) 46.21 (12.34)	3.56 2.59	<0.001 0.01	0.50 0.37

Note. *df*=205 (parent ratings); *df*=205 (teacher ratings).

These results suggest that the impairments on executive tasks administered to very preterm children in a laboratory setting are also observed by parents and teachers in more everyday contexts and activities. While parents and teachers reported difficulties in all areas, the effect sizes were higher in the cognitive aspects of executive control, such as planning, initiation and working memory (d=0.38-0.68), while those for emotional control and inhibitory control were somewhat lower (d=0.20-0.35).

7.7 Examiner Behavioural Ratings

Examiner observations of executive behaviour during children's developmental assessments showed that children in the very preterm group demonstrated lower levels of initiative, $\chi^2(3) = 28.71$, $p<0.001$; inhibitory control, $\chi^2(3) = 17.66$, $p<0.01$; sustained attention, $\chi^2(3) = 11.41$, $p<0.05$; self-monitoring, $\chi^2(3) = 27.62$, $p<0.001$; and strategising and planning of their problem-solving responses, $\chi^2(3) = 26.53$, $p<0.001$. Thus, across all examiner ratings, children in the very preterm group showed less evidence of exercising executive behaviours during their assessments.

Exclusion of Scores of Children with Cognitive Impairment or Severe Cerebral Palsy. All between-group differences on behavioural rating scales remained significant ($p<0.05$) when children with neurodevelopmental impairments were excluded from analysis, suggesting that the impaired performance on these measures could not be attributed to low scores in a small number of children with more severe impairments.

7.8 Control for Socioeconomic Selection Factors

The above findings suggest the presence of pervasive impairments in executive function in children born very preterm, with these difficulties evident across multiple executive domains and ecological contexts. However, it is possible that these associations may have arisen due to social selection factors associated with very preterm birth. As shown in Table 5.1, children born very preterm were more likely to have come from to come from families with greater financial stress and lower socio economic status levels than those in the full term group. This financial stress and its consequences may have impacted on the cognitive development of children in the very preterm group.

In order to examine the influence of socio economic selection factors on the performance of each group, univariate ANCOVAs were performed with gestation group (very preterm or full term) entered as a fixed factor and the highest level of SES in the family (as determined by the Elly-Irving scales) entered as a covariate on selected measures of executive function. Where dependent variables were categorical, logistic regression analyses were completed with the same covariate. The adjusted marginal means and effect sizes after controlling SES are reported in Table 7.7.

As is clear from this table, while group differences in performance were attenuated after consideration of SES, differences in mean performance continued to be significant and in favour of the full term group for the backwards Corsi Blocks trials ($p<0.05$), Tower of Hanoi total score ($p<0.05$), Visual Search accuracy ($p<0.05$) and K-CPT errors of omission and errors overall ($p<0.05$). Bivariate logistic regression analyses showed that children in the preterm group showed a greater tendency to fail to understand the criterion backward Digit Span task trials, OR= 3.07 (0.93-10.10) $p<0.01$; were more likely to fail due to rule breaks on the Tower of Hanoi Task, OR = 2.59 (1.36-4.95), $p<0.01$; and were more likely to fail the third phase of the Detour Reaching Box task, OR=15.17 (1.88-122.18), $p<0.01$ after covariate adjustment for SES.

Based on these covariate models, it appears that children in the very preterm showed discrepancies in performance in a number of areas of executive function and that these discrepancies were apparent even after accounting for between-group socio economic differences. In particular, spatial working memory and sustained attention have the largest effect sizes, suggesting that these may be particular areas of difficulty in this population. In contrast, the difference in performance on the measure of verbal working memory is small and children in both groups achieved similar span levels, even though children in the very preterm group passed fewer trials. Given that these difficulties in executive function appear so pervasive, a more detailed investigation of the particular background characteristics of these children and how they may influence individual performance on these tasks is warranted in order to determine what specific individual characteristics are contributing to these impairments.

Table 7.7: Adjusted Means and Effect Sizes for Performance on Laboratory Measures of Executive Function in Children Born Very Preterm and Full Term after Controlling for Group Differences in Family Socioeconomic Status

	Group				
Executive Function Measure	Very Preterm (n=103)	Full Term (n=108)	Adj. F	p	Adj. effect size (*d*)
Measures of working memory					
Raw score Digit Span forward	5.93	6.17	2.47	0.12	0.17
Forward Digit Span	4.26	4.36	0.80	0.37	0.18
Raw score Digit Span backward	4.57	4.89	2.85	0.09	0.24
Backward Digit Span	2.69	2.74	1.02	0.31	0.03
Raw score Corsi Blocks forward	5.45	5.66	0.80	0.37	0.12
Forward Corsi Blocks Span	3.27	3.32	0.12	0.73	0.05
Raw score for Corsi Blocks backwards	2.64	3.26	10.28	<0.01	0.44
Corsi Blocks backwards span	2.61	2.91	5.84	0.02	0.35
Measure of planning/problems solving					
Tower of Hanoi total score	3.14	3.80	4.81	0.03	0.31
Measure of selective attention					
Visual search accuracy score (correct responses-errors)	20.69	24.64	7.04	0.009	0.37
Visual search time to complete trials	188.77	210.47	5.95	0.02	0.37

Measure of sustained attention and inhibitory control					
CPT Trials completed	188.96	195.29	3.15	0.08	0.29
CPT % Errors of omission over trials where response was required	21.08	13.84	11.94	<0.001	0.49
CPT % Errors of commission over inhibition trials completed	36.69	44.07	8.19	0.005	0.40
CPT Response time	623.20	591.50	3.38	0.07	0.28
CPT % Total errors	24.98	21.40	4.93	0.03	0.33

Chapter 8

Results 3: Relationships between Measures of Executive Function at Age 6 years

Results thus far indicate that by age 6 years of age, children born very preterm show impairments in several areas of executive function, spanning verbal working memory, spatial working memory, cognitive flexibility and attentional control. Furthermore, these difficulties were observed across multiple contexts and sources. Whilst there was some suggestion that the manipulation of information in spatial working memory may pose a greater challenge than verbal information for children born very preterm, more generally, group discrepancies across multiple measures tended to suggest the presence of pervasive impairments in executive function as opposed to a highly specific pattern of impairments in one or two domains.

This diffuse pattern of impairment across tasks and domains supports the theoretical model of executive function as a common, underlying construct measured by these tasks (Elliot, 2003; Hughes et al., 2004; Lezak, 1983). Given the suggestion of a consistent pattern of global impairment across key laboratory measures in chapter 7, it was deemed appropriate to explore the extent to which these measures might load on a single, common factor or smaller set of factors tapping children's executive functioning abilities. This is a common research practice in developmental studies of executive function, with findings suggesting that individual executive tasks, when combined, can often elucidate underlying executive domains (Carlson, Mandell, & Williams, 2004; Carlson, Moses et al., 2004; Taylor, 2002; Welsh et al., 1990). Another advantage of creating larger composite measures of children's executive function is that such measures help to minimise the effects of measurement error associated with individual tasks as well as fatigue and concentration lapses that invariably happen when assessing young children. As well as offering measures of executive function that are more psychometrically robust, the creation of summary measures based on children's performance across multiple measures would also allow for a more parsimonious analysis of the risk factors associated with later executive function impairment and the implications of executive difficulties for school functioning.

To assess the feasibility of combining task scores, three sets of analyses were undertaken. First, bivariate patterns of association between children's overall performance on each of the six laboratory measures were examined using Pearson's correlations. For this analysis, children's overall categorical rankings (1-4) for each task were examined. This was because children's task completion was often dependent on their ability to overcome earlier task demands. Thus, the use of raw scores would not sufficiently capture performance. Following this, the extent to which these measures might be tapping overlapping or common aspects of executive function was examined using Principle Components Analysis (PCA). Principal components analysis allows for a more precise description of correlations among variables by extracting the shared variance among them, thereby suggesting a latent or underlying factor that they may be assessing (Bartholomew, Steele, Moustaki, & Galbraith, 2002; Comrey & Lee, 1992). Thus, PCA allows a large number of variables to potentially be summarised or reduced to smaller set of underlying factors or constructs. This form of factor analysis was chosen because the primary aim of this analysis was to reduce the data to a more manageable set of indicators of executive function, while retaining as much of the variance in the data as possible. In practice, principal components analysis often yields similar results to other factor extraction methods (Meyers, Gamst, & Guarino, 2006).

For the PCA, three sets of indicators were considered. First, the total amount of variance across all tasks that the factors explained, as indicated by the eigen value associated with each factor, was examined. The eigen value is technically defined as the sum of squared correlations for each score in relation to the factor (Meyers et al., 2006). Thereafter, the communalities, representing the relationship between individual task scores and all other variables were considered. As impairments were seen across most of the executive function measures, it was deemed preferable that the variance extracted from each measure be relatively equal and substantial. Communalities that were very low were re examined (Meyers et al., 2006). Finally, the factor item loadings, representing the individual contributions (or weight) of each variable to the factor were also taken into consideration. A factor loading cut-point of 0.3 was used to determine whether factors were viable (Carlson, Mandell et al., 2004).

To confirm that the interpretation of the PCA was theoretically valid, the results were further tested using confirmatory factor analysis. This analysis was performed using the AMOS statistical program in combination with SPSS. Confirmatory factor analysis tests the viability of the proposed factor models by estimating the strength of unknown relationships and testing these estimated relationships against the observed, known correlations between variables. A sufficient match between the predicted and observed correlations is indicative of a good model fit. Four fit indexes were considered for this analysis. The Chi-square tests the differences between the observed and estimated models. If this difference is sufficiently large, the Chi-square will be significant, indicating poor model fit. However, the chi-square test is not as suitable for sample sizes >200, because it is too powerful (Meyers et al., 2006). Thus, the Root Mean Square Error of Approximation (RMSEA), which tests the residual variance between the two models, was also examined. An RMSEA index below 0.08 indicates satisfactory fit. Finally, the Comparative Fit Index (CFI) and Normed Fit Index (NFI) were examined. These statistical tests compare the theoretical estimates of relationships against a model that assumes no relationships between variables. CFI and NFI values above 0.9 indicate good model fit (Meyers et al., 2006).

8.1. Correlations between Measures of Executive Function

Correlations between children's performance on each of the executive function measures administered during children's 6 year laboratory assessment are shown in Tables 8.1 and 8.2. These correlations are shown for 1) the total sample (Table 8.1), 2) the very preterm group only, and 3) the full term group only (Table 8.2). Across all analyses, the six executive function measures were significantly intercorrelated (*r* =.19-.48). In addition, there was a tendency for measures assessing working memory, such as the Digit Span and Corsi Blocks tasks, to be more strongly correlated with each other (*r* = 0.48) than with other measures (*r* = 0.19-0.39). Similarly, there was a tendency for measures assessing attentional control and flexibility, such as the CPT and Detour Reaching Box, to be more strongly correlated with each other. More complex, multidimensional tasks such as the Tower of Hanoi and Visual Search Task, showed similar, moderate correlations with all other measures (*r* = 0.28-0.43). These patterns were particularly evident in the very preterm group, whereas the correlations in the full term group were less specific (*r* = 0.07-0.39). Correlations using non-parametric Spearman's rho tests were very similar.

Table 8.1: Correlations between Performance Scores for Measures of Executive Function in Children Born Very Preterm and Full Term at Age 6 Years

	Digit Span	Corsi Blocks	Tower of Hanoi	Visual Search	CPT
Digit Span					
Corsi Blocks	.48				
Tower of Hanoi	.30	.32			
Visual Search	.43	.39	.37		
K-CPT	.19	.29	.34	.28	
Detour Reaching Box	.22	.20	.32	.34	.33

Note. All correlations, p<0.01

8.2 Principal Components Analysis of Associations between Tasks

Since visual inspection of the bivariate associations between executive function measures suggested that tasks were associated, an analysis of this data using principal components analysis (PCA) was undertaken. This analysis was run for 1) the preterm and full term groups combined, 2) the preterm group separately, 3) the full term group separately. Although not shown, analyses using continuous measures from each executive task were consistent with those reported below. The first PCA, based on the total sample, produced one factor score explaining 42% of the total variance. The Bartlett's test of sphericity was significant, indicating that the correlations among these tests were sufficient for factor analysis (Meyers et al., 2006).The eigenvalue for this factor was 2.54 and factor loadings were all above 0.6. However, the communalities for both the Detour Reaching Box task and the CPT were low (0.36) indicating that, as the correlation matrix had suggested, these tasks were not as strongly associated with the working memory measures. As the overall variance extracted by this single factor was also low (<50%), a two factor-solution was considered preferable. This two-factor solution explained 59% of the total variance. Communalities were high (0.45-0.73). A generally consistent pattern of findings was obtained from factor analyses based on the very preterm and full term samples.

Table 8.2: Correlations between Executive Function Performance Scores for Children Born Very Preterm (black) and Full Term (blue)

	Digit Span	Corsi Blocks	Tower of Hanoi	Visual Search	CPT	Detour Reaching Box
Digit Span		.38	.21	.39	.07	.23
Corsi Blocks	.57		.26	.26	.22	.10
Tower of Hanoi	.34	.33		.27	.31	.21
Visual Search	.43	.33	.41		.31	.25
K-CPT	.23	.26	.32	.15		.24
Detour Reaching Box	.18	.21	.27	.34	.27	

The final, rotated factor loadings for the whole sample and each separate study group (very preterm, full term) are shown in Table 8.3. Consistent with the theoretical understanding that factors would be correlated, an oblique, direct oblimin rotation was performed. Results show that, as had been indicated by the correlational analyses, the two working memory tasks (Digit Span and Corsi Blocks) appeared to cluster together, with loadings above 0.7 on the first factor, whilst the Detour Reaching Box and CPT tended to cluster together, with loadings above 0.7 on the second. The two remaining tasks (the Tower of Hanoi and Visual Search) appeared to contribute to both factors, with rotated loadings above 0.3 on both factors. In the very preterm group, these tasks loaded more consistently with the first, working memory factor. The pattern was slightly different in the full term group. The working memory measures appeared to cluster on a single factor once rotated. However, the distinction between working memory measures and the Detour Reaching Box and K-CPT tasks appeared robust.

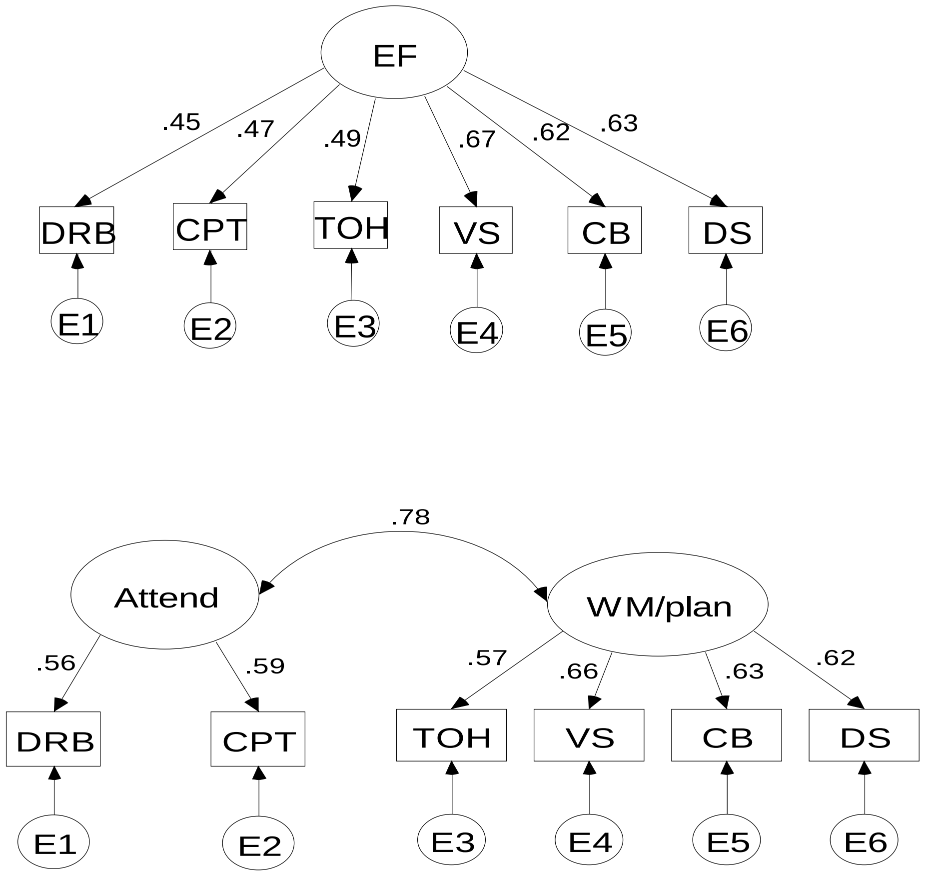
Collectively, the results from both bivariate correlational analyses and the PCA indicated that, although there were inter-correlations between all executive function tasks, possibly reflecting a common latent executive function construct, tasks that had been selected to tap more ‘cool,’ cognitive working memory and sequencing processes appeared to be more strongly related whilst more behaviourally-based, sustained attention and motor switching abilities appeared to be more closely associated. The two more complex tasks (Tower of Hanoi and Visual Search) possibly incorporated elements of both factors but, in the very preterm group in particular, were more robustly associated with the working memory tasks. The variance explained by the division of these tasks into two dimensions (approximately 60%) was much higher than that explained by the single executive composite (40%), suggesting that two summary scores, incorporating these two dimensions, would best reflect children’s overall performance across executive measures.

Table 8.3: Factor Loadings from a Principal Components Analysis of Measures of Executive Function in Children Born Very Preterm and Full Term

	Group					
	Full sample		Very Preterm		Full Term	
Digit span backwards	.88	-.10	.88	-.11	-.86	-.18
Corsi Blocks backwards	.82	-.06	.83	.09	-.76	.00
Tower of Hanoi	.33	.39	.47	.33	.05	.65
Visual search accuracy	.47	.37	.61	.20	-.34	.53
Detour Reaching Box	.12	.85	.10	.89	-.13	.56
K-CPT	.02	.75	.08	.64	.15	.79

8.4 Confirmatory Factor Analysis

In order to determine whether a two-factor model of executive function was viable, confirmatory factor analyses were performed for each model across 1) the full sample, including very preterm and full term children, 2) the very preterm group, 3) the full term group. The two different models tested can be seen in Figure 8.1, together with the standardised factor loadings for the whole sample. The results for the analysis of a one factor and two-factor models can be seen in Table 8.4. Similar to results from the PCA, these confirmatory analyses suggested that both models of executive function were acceptable, with indexes of model fit being relatively equal. The RMSEA indices for all models were below 0.08, suggesting a good model fit for all models tested across the groups (Meyers et al., 2006). The two factor solution showed that the correlation between the two measures was high, but that the loadings for the Detour Reaching Box and Continuous Performance Task were slightly higher for the two factor solution. Given that PCA had suggested that more variance could be explained by the second, two factor-model of the data, this model was considered to be a more robust indicator of executive performance. Thus, two summary scores, incorporating 1) working memory and planning and 2) attention control and flexibility measures, were created.



EF: Executive function, DRB: Detour Reaching Box, CPT: Kiddie's- Continuous Performance Task, TOH: Tower of Hanoi, VS: Visual Search, CB: Corsi Blocks, DS: Digit Span.

Figure 8.1: One Factor and Two Factor Models of Executive Function Tested in Confirmatory Factor Analysis

Table 8.4: Indexes of Model Fit for Confimatory Factor Analyses of Single and Two-Factor Executive Function Models

	Group		
	Full sample (n=211)	Very preterm (n=103)	Full Term (n=108)
Single Executive Function Factor Model			
Chi-square (df) p	18.75 (9), 0.03	14.88 (9), 0.09	10.3 (9), 0.33
NFI	0.91	0.87	0.86
CFI	0.95	0.94	0.98
RMSEA	0.07	0.08	0.04
Two-Factor Model			
Chi-square (df) p	17.38 (8), 0.03	11.99, (8), 0.15	12.25 (8), 0.14
NFI	0.92	0.90	0.85
CFI	0.96	0.96	0.93
RMSEA	0.08	0.07	0.07

Note. An RMSEA of <0.08 indicates a satisfactory fit, while an RMSEA above 1 indicates poor fit.
A chi-square value that is significant indicates that the model does not fit the data well. However, the Chi-square is sensitive to sample size. When the sample size is >200, it is generally significant even if the model fits the data well (Kenny, 2003).
CFI/NFI - A value >0.9 indicates a good fit, while <0.6 indicates a poor fit.

8.4 Creation of Composite Scores

To form the composite executive function measures, children's performance scores on each task loading on each of the two factors were summed. The scores for the Corsi Blocks backward span task, the backwards Digit Span, the Tower of Hanoi and the Visual search tasks were summed to form a working memory/planning composite and the Detour Reaching Box and CPT omission error measures were summed to form an executive attention composite. Scores were not weighted because this may have attributed disproportionate importance to measures that were correlated more with the underlying construct, rather than reflecting children's overall performance across all the tasks. For the 15 children for whom data from the CPT task was missing due to computer difficulties, task refusal or being unable to complete the task, their score for the executive attention composite was imputed using a regression method (McKnight, McKnight, Sidani, & Figueredo, 2007)[1]. In the case of the working memory/plan composite, few cases (n=2) were missing any data, with missing data generally being the result of misunderstanding the task or the child declining to complete the task. In these cases, scores were allocated based on previous performance on these measures at 4 years, the reasons for the loss of data (e.g. misunderstanding the task instructions would indicate lower ability) and performance across the other executive function measures. One child was not allocated an executive attention score because they had refused to undertake either of these tasks.

8.5 Comparison of Very Preterm and Full Term Groups on Composite Factor Scores

To illustrate the overall performance of children of the two study groups on these composite measures of executive function Table 8.5 shows the mean scores on the working memory/sequencing and executive attention composites for groups of children born very preterm and full term. As shown in this table, groups differed significantly in performance on both of these composite scores, with children born very preterm gaining scores between half a standard deviation and one standard deviation below those born full term. These differences remained even after children with severe neurodevelopmental impairment were excluded from the analysis.

[1] For the executive attention composite, 14 (7 for each group) children had refused to complete or did not have data for the CPT task. Therefore, children's scores were imputed using a regression-based method (McKnight et al., 2007). Scores from measures that were not included in either executive composite were selected as the use of variables that are included in the analyses can lead to an inflated relationship. The most highly correlated independent measures were the examiner ratings of sustained attention (0.58) and inhibitory control (0.61). The regression equations gained from these predictor measures was used to predict executive attention scores for these children. The regression equation for the very preterm group was y= 1.57 + (0.75*behaviour rating of

Table 8.5: Performance of Children Born Very Preterm and Full Term on Composite Measures of Executive Function

	Very Preterm (n=102)	Full Term (n=108)	t	p	*d*
Working Memory/Sequencing Factor	9.86 (2.70)	11.30 (2.33)	4.15	<0.001	0.57
Executive Attention Factor	5.25 (1.61)	6.43 (1.33)	5.74	<0.001	0.78

Note. df=195-207

These analyses provide support for the conceptualisation of these tasks as capturing two broad, inter-related domains of executive function in children born very preterm. Specifically, tasks that involved the maintenance of information in working memory and the planning of responses on the basis of such information were grouped on one dimension, while those tasks that involved the ability to maintain focus and flexibly inhibit and alter responses according to stimuli were grouped on another. On both of these dimensions of executive function, children in the very preterm group performed less well than those in the full term group. These findings raise the important question of why very preterm children experience these later executive difficulties. Accordingly, the next chapter will focus on the risk factors and life course processes that place very preterm children at elevated risk of later working memory/planning and executive attention problems at early school age.

inhibitory control) + (0.63*behaviour rating of sustained attention). All subsequent analyses pertaining to this factor score were checked to ensure that findings were consistent when these children were excluded.

Chapter 9:

Results 4: The Role of Medical, Neurological and Socio-Familial Factors in Accounting for Individual Differences in Executive Performance Amongst Children Born Very Preterm

Results from chapter 7 suggested that children born very preterm were more likely to show pervasive difficulties in executive function when compared to a group of full term control children. Further analyses indicated that tasks on which children born very preterm showed difficulties appeared to tap two broader domains of executive function; specifically 1) working memory and planning and 2) executive attention. However, it is also clear that there was considerable variability in the performance of children born very preterm and that not all of these children were experiencing difficulties. This is evident from the fact that 30-60% of children in the very preterm group achieved scores of 3 or 4 on one or more of the executive function measures, indicating performance that was similar to that of the full term group. In addition, 10% of children in the very preterm group consistently achieved scores of 3 or greater for all of these tasks.

This variability in individual performance within the very preterm group raises questions about the clinical and developmental mechanisms that place some children born very preterm at risk of executive impairment. Very preterm birth is correlated with several medical, neurological and socio-familial risk factors that are likely to play an important role in the genesis of executive impairments. Accordingly, the third aim of this thesis was to examine the extent to which a range of individual medical, neurological and social factors were associated with children's later performance on measures working memory/planning and executive attention.

Because this chapter aimed to provide an understanding of individual differences in performance within children born very preterm, this analysis was confined to the very preterm group. Based on findings from previous studies, four sets of factors were considered. First, indicators of perinatal history and clinical characteristics, including gender, gestation, birthweight, IUGR and a number of medical conditions were considered. Second, indicators of early neurological development, including MRI measures of white and grey matter abnormality, PVL and IVH, were examined. Third, potentially influential socio-familial background factors, such as SES and family composition, were considered while the fourth set consisted of indicators of family functioning over the first 6 years of life, including changes in parents, maternal depression and anxiety, parenting style and stressful life events.

Data analysis was undertaken in two stages. First, relationships between each set of factors and the dependent working memory/planning and executive attention composite scores were examined using t-tests and one-way ANOVA. These tests allowed for the identification of any significant relationships between independent risk factors and continuous executive function scores, thereby guiding the selection of variables for the next part of the analysis. Second, in order to identify the best, independent medical, neurological and socio-familial predictors of children's working memory and executive attention scores at age 6 years, relationships were modelled using multiple linear regression. Multiple linear regression allows for the description of the relationship between an independent and dependent variable in the context of several other independent variables (Cohen, Cohen, West, & Aiken, 2003). The results of these analyses are described below.

9.1. Associations between Antecedent Clinical, Neurological and Socio-Familial Factors and Children's Later Working Memory/Planning Performance

Neonatal Clinical Factors Associated with Later Working Memory/ Planning Performance in Children Born Very Preterm. Table 9.1 describes associations between a range of infant medical risk factors assessed during the perinatal period and children's subsequent total working memory/planning scores. Correlations between the various medical factors and later working memory/planning scores are also provided in Table 1 of Appendix E. Infant medical risk factors examined included gender, gestational age, birthweight, twin/single birth status, IUGR, maternal smoking during pregnancy, maternal antenatal steroids, evidence of maternal infection, maternal postnatal steroids, days on respiratory support, RDS, CLD, PDA, ROP, NEC, infant sepsis and postnatal steroid administration.

The results in Table 9.1 show that boys obtained lower overall scores on this composite measure of executive working memory/planning than girls ($p<0.01$). In addition, children born to mothers who showed evidence of infection (chorioamniotis or fever) at the time of birth generally obtained lower scores ($p<0.05$). There was also a tendency for the amount of ventilatory support, recorded as days spent on CPAP and/or IPPV, to be associated with working memory/planning scores. However, this association did not quite reach significance ($p<0.10$). No other infant clinical risk factors were found to be associated with working memory/planning at age 6 years.

Table 9.1: Relationships between Perinatal Clinical Factors and Executive Working Memory/Planning at Age 6 Years Amongst Children Born Very Preterm

Clinical Factors	N	Mean (SD) Executive Working Memory/ Plan Score	F/t	p
Gender				
Male	53	9.03 (2.75)		
Female	49	10.76 (2.35)	3.40	0.001
Gestational age				
23-26 weeks	26	9.35 (2.13)		
27-28 weeks	23	9.68 (3.25)		
29-34 weeks	43	10.30 (2.52)	1.13	0.33
Birthweight				
<750g	17	9.78 (2.69)		
750-1000g	25	10.00 (2.57)		
>1000g	60	9.82 (2.80)	0.55	0.58
Multiple birth				
Twin	34	10.44 (2.58)		
Singleton	68	9.56 (2.72)	1.56	0.12
IUGR				
Yes	11	9.85 (3.36)		
No	91	9.86 (2.64)	0.01	0.99
Maternal smoking during pregnancy				
Yes	39	10.15 (2.63)		
No	62	9.56 (2.72)	1.56	0.33
Maternal antenatal steroids				
Yes	85	9.96 (2.68)		
No	17	9.35 (2.83)	0.84	0.40

Table 9.1: Relationships between Perinatal Clinical Factors and Executive Working Memory/Planning at Age 6 Years Amongst Children Born Very Preterm

Clinical Factors	N	Mean (SD) Executive Working Memory/ Plan Score	F/t	p
Maternal chorioamniotis/fever				
Yes	14	8.29 (2.55)		
No	87	10.11 (2.65)	2.46	0.02
Respiratory distress syndrome				
Yes	85	9.80 (2.77)		
No	17	10.12 (2.39)	0.44	0.66
Days of respiratory support (CPAP + IPPV)				
None	7	10.86 (1.86)		
1-10 days	43	10.26 (2.56)		
11-30 days	19	9.23 (3.04)		
30+ days	33	9.48 (2.60)	1.19	0.32
Chronic lung disease				
Yes	34	10.01 (2.47)		
No	68	9.78 (2.82)	0.41	0.67
Patent ductus arteriosis				
Yes	45	9.84 (2.65)		
No	57	9.86 (2.76)	0.04	0.97
Retinopathy of prematurity				
Yes	36	10.17 (2.74)		
No	65	9.31 (2.60)	1.53	0.13
Necrotising entercolitis				
Yes	7	8.57 (1.81)		
No	95	10.06 (2.67)	1.04	0.30

Table 9.1: Relationships between Perinatal Clinical Factors and Executive Working Memory/Planning at Age 6 Years Amongst Children Born Very Preterm

Clinical Factors	N	Mean (SD) Executive Working Memory/ Plan Score	F/t	p
Proven sepsis in infant				
Yes	30	9.44 (2.79)		
No	71	10.06 (2.67)	1.04	0.30
Postnatal steroids				
Yes	11	9.55 (3.11)		
No	91	9.90 (2.66)	0.40	0.69

Note. df=100

Neonatal Neurological Factors Associated with Later Working Memory/ Planning Performance in Children Born Very Preterm. Table 9.2 shows the relationships between measures of early cerebral abnormality and children’s executive working memory/planning performance at age 6 years. Correlations are also provided in Table 2 of Appendix E. Neurological measures included diagnoses of IVH and PVL from serial ultrasound scans performed during the children’s time in the NICU and qualitative ratings of cerebral white and grey matter abnormalities from MRI scans performed at term equivalent age.

Clear associations were found between the extent of early neurological abnormality and children’s composite working memory and planning scores at age 6 years. In particular, with increasing severity of IVH, children were more likely to achieve lower working memory/planning scores ($p<0.001$). Children with evidence of PVL also obtained lower scores ($p<0.01$). Similarly, the extent of white matter abnormality on MRI was significantly related to later performance on the working memory/plan composite, with increasing severity of white matter abnormality being associated with poorer working memory/planning performance at age 6 years ($p<0.01$). There were no significant associations between the extent of grey matter abnormality, predominantly gyral delay, and children's working memory/planning scores at age 6 years. These findings suggest that early injury or disruption of the developing cerebral white matter may have ongoing implications for working memory development.

Table 9.2: Relationships between Term Equivalent Neurological Measures and Executive Working Memory/Planning at Age 6 Years Amongst Children Born Very Preterm

Neurological Factors	N	Mean (SD) Working Memory/ Plan Factor Score	F/t	p
Severity of IVH (ultrasound)				
No IVH	73	10.36 (2.62)		
Grade I/II IVH	21	9.00 (2.62)		
Grade IV/V IVH	5	6.80 (1.92)	5.96	0.004
PVL (ultrasound)				
Yes	5	6.80 (2.95)		
No	96	10.01 (2.62)	2.66	0.009
White matter abnormality (MRI)				
None (Score <7)	22	10.36 (2.59)		
Mild (7-9)	60	10.27 (2.62)		
Moderate /severe (• 10)	19	7.95 (2.39)	6.42	0.002
Grey matter abnormality (MRI)				
None (Score<5)	42	10.32 (2.69)		
Mild (5-6)	35	9.77 (2.44)		
Moderate/severe (>7)	24	9.17 (3.07)	1.41	0.25

Note. df=100

Socio-Familial Factors Associated with Later Working Memory/Planning Performance in Children Born Very Preterm. Table 9.3 describes relationships between selected measures of family circumstances and the composite working memory/planning factor at age 6 years. Measures of children’s family background included SES (recorded at 2 or 4 years), maternal age at term and whether the child was born into a single parent family. Measures of family functioning included the number of parental changes the child had experienced, maternal depression and anxiety from 1 through 6 years, total stressful life events experienced from 1 through 6 years and observational measures of parenting behaviours, including maternal sensitivity, intrusiveness and parent-child interactional synchrony, rated from video-recorded problem-solving interactions between each child and their caregiver at ages 2 and 4 years. For illustrative purposes, children have been divided into groups according to their scores on these measures. Correlations between these measures of socio-familial background and working memory/planning performance are also shown in Table 3 of Appendix E.

As shown in Table 9.3, in terms of the family background factors, children from families with lower SES ($p=0.05$) and lower income households tended to achieve lower executive performance scores ($p<0.01$). No other measures of family background were significantly associated with children's later performance. In terms of family functioning, children who had experienced a change in parent, generally through parental divorce or separation, obtained lower scores on working memory/planning tasks ($p<0.01$). Additionally, all three measures of maternal-child interaction were significantly associated with children's later working memory/ planning scores. Specifically, children with mothers who were less sensitive during the problem-solving tasks at ages 2 and 4 tended to obtain lower scores than those whose mothers had shown higher levels of sensitivity ($p<0.01$). Similarly, children whose mothers had been intrusive and controlling during these interactions obtained lower working memory/planning scores at age 6 years ($p<0.01$). Finally, in terms of the reciprocal nature of the parent-child relationship, children who had shown high levels of interactional synchrony with their parents during the same interactions were more likely to obtain higher scores on the task measures of working memory and planning ($p<0.05$). Other measures of family functioning, including measures of maternal psychological wellbeing and family stress, were not significantly related to children's working memory/planning performance at age 6 years. Collectively, these findings suggest that some family background factors, primarily low financial resources and parental instability, may increase the risk of later working memory/planning impairments in children born very preterm. However, the most robust associations appear to be related to parenting. Children who had experienced sensitive, non-intrusive, reciprocal interactions with their parents during early childhood tended to show better performance on working memory/planning tasks at age 6 years.

Table 9.3: Relationships between Socio-Familial Factors and Executive Working Memory/Planning at Age 6 Years Amongst Children Born Very Preterm

Socio-Familial Factors	N	Mean (SD) Working Memory/ Plan Factor Score	F/t	p
Family background				
Family SES (2/4 yrs)				
Manual/unemployed	11	8.0 (2.72)		
Semi-skilled/some qualifications	66	10.14 (2.64)		
Professional/managerial	25	9.92 (2.63)	3.10	0.05
Income (6 years)				
< $NZ 25 000	19	8.05 (2.59)		
• $NZ 25 000	83	10.27 (2.56)	3.39	0.001
Maternal age (Term)				
<25 years	12	9.50 (3.32)		
• 25 years	90	9.90 (2.62)	0.49	0.63
Family structure (Term)				
Single parent	19	9.00 (2.89)		
Defacto/married	83	10.05 (2.63)	1.54	0.13
Family functioning				
Parental change (Term - 6 years)				
No change in parent	72	10.34 (2.57)		
At least 1 parental change	22	8.94 (2.68)		
>1 change	8	8.20 (3.08)	4.16	0.02

Socio-Familial Factors	N	Mean (SD) Working Memory/ Plan Factor Score	F/t	p
Maternal depression (1-6 years)				
None	58	9.90 (2.51)		
1 episode	29	9.86 (3.02)		
>1 episode	14	9.67 (3.04)	0.04	0.96
Maternal anxiety (1-6 years)				
None	52	10.13 (2.48)		
1 episode	26	9.81 (3.03)		
>1 episode	24	9.31 (2.80)	0.77	0.46
Family stress (1-6 years)				
Mild stress (<10)	52	10.04 (2.99)		
Moderate stress (10-20)	26	9.67 (2.44)		
High stress (>20)	23	9.65 (2.40)	0.24	0.79
Parent supportive presence (2 & 4 years)				
Low (1)	24	8.58 (2.89)		
Moderate (2-3)	62	10.15 (2.67)		
High (>3)	14	10.93 (1.73)	4.36	0.02
Parent intrusiveness (2 & 4 years)				
Low (1)	52	10.65 (2.38)		
Moderate (2-3)	33	9.56 (2.82)		
High (>3)	15	7.93 (2.63)	6.93	0.002
Parent-child synchrony (2 & 4 years)				
Low (<2.5)	32	8.73 (3.14)		
Moderate (2.5 -3.5)	52	10.44 (2.51)		
High (>3.5)	17	10.29 (1.65)	4.51	0.01

Note. df=100

9.2. Predictors of Executive Working Memory/Planning Performance in Children Born Very Preterm

The existence of these associations introduces questions as to their collective or interactive patterns of influence. To examine the factors that best predicted performance on the working memory/planning composite, significant correlates of children's working memory/planning scores were entered into a series of multiple linear regression models to examine which factors made significant net contributions. Independent variables were entered in a block recursive fashion, with antecedent clinical factors entered first, neurological factors entered second and measures of family background and function entered last. This allowed for the examination of possible mediational effects on antecedent clinical risk factors by factors entered later in the model.

As the aim of this analysis was to determine the most important predictors of later working memory/planning performance, modelling was undertaken using a forwards and backwards approach. In terms of the forwards approach, for each stage of the model, the most highly correlated variables were entered first, followed by the remaining predictors, in order of their degree of correlation. Where predictors were not significant ($p<0.1$), they were not retained in future analyses. Forwards models were then confirmed using a backwards approach. For this approach, all significant variables were entered for each stage of the model and those that contributed least variance were eliminated until the most parsimonious model had been indentified (Meyers et al., 2006). Wherever possible, independent variables were entered as continuous measures (Pagano, 1990). Where variables were necessarily categorical, dummy codes were used (e.g. male =1, female = 0). Interactions among these variables were also considered by creating multiplicative terms and entering these with the independent predictors (Cohen et al., 2003).

The regression models are described in Table 8.9. Key statistics reported for the overall models are 1) the F-statistic, indicating the ratio of variance attributable to the independent predictors versus that attributable to error (Cohen et al., 2003), 2) the significance level, indicating whether the combination of independent predictors explains a significant amount of variance in the dependent variable, 3) the squared multiple correlation (R^2), indicating the proportion of the dependent variable's variance that overlaps with that of the combination of independent variables (Cohen et al., 2003; Meyers et al., 2006). In addition, for each significant ($p<0.1$) independent variable, the table also reports 1) the unstandardised regression coefficient (B), which indicates the amount of change in the specific independent variable that is associated with change in the dependent variable, 2) the standardised beta coefficient (•), which indicates the partial prediction of the independent variable on the dependent variable when all variables are standardised 3) the standard error of estimation (SE), which is the standard deviation of the residual variance after prediction and 4) the t-test p-value, indicating whether the independent variable is significantly associated with the dependent variable after controlling for other predictors (Cohen et al., 2003; Leech, Barret, & Morgan, 2005; Meyers et al., 2006).

As can be seen from this table, results identified two antecedent clinical risk factors as being associated with later working memory/planning performance. Specifically, being male ($p=0.001$) and having been exposed to maternal infection (chorioamniotis or maternal fever) placed one at greater risk of impaired working memory/ planning performance at age 6 years ($p<0.01$). No significant interactions were found between gender and maternal infection.

Addition of neurological factors revealed a significant association between the total, qualitatively-rated cerebral white matter abnormality score at term age and their later performance on working memory/planning tasks ($p<0.001$). Specifically, increasing severity of white matter abnormality was associated with lower scores on these tasks. While the inclusion of the white matter abnormality score in this second model led to a small attenuation in the unstandardised and standardised regression coefficients for the clinical variables (gender and infection), these variables continued to be significant in the model, suggesting an independent contribution of each. Further tests suggested no significant interactions between white matter abnormality and gender, white matter abnormality and infection or all three of these variables.

Finally, consideration was given to the early life experiences that may have had potential influence on children's cognitive development by age 6. During the third phase of modelling, family background factors were considered. None of these factors significantly contributed to the model. During the forth phase of modelling, family functioning factors were considered. This analysis showed that children's experience of parental change was significantly related to their subsequent performance on the working memory/planning measure. Children who had experienced a change in parent generally achieved lower scores on this measure ($p<0.05$). Parent-child interactional synchrony was significantly associated with working memory performance ($p<0.05$). Once interactional synchrony between the child and parent was considered, the effect of white matter abnormality was attenuated, suggesting potential mediation of white matter abnormality by the level of synchrony between parent and child.

Following consideration of each of these influences, further tests for interaction were conducted. Potential interactions tested included gender and the experience of parental change, gender and interactional synchrony, white matter abnormality and synchrony, infection and parental change, infection and parent-child synchrony and multi-level combinations of all of the above. None of these interaction terms were significant ($p>0.05$), suggesting that each of the predictors shown in the models contributes additively to working memory/planning difficulties in children born very preterm. Plots of the residual variances for each of these models indicated no departure from normality, supporting the specificity of this model. Thus, it appears that maternal infection and white matter abnormalities were the strongest early predictors of children's working memory/planning at age 6, but that a consistent, synchronous relationship with a parent is also important. Together, these independent variables were able to predict a moderate proportion of the variance (approximately 30%) in the working memory/planning performance of children born very preterm at age 6 years.

Table 9.4: Medical, Neurological and Socio-Familial Predictors of Later Working Memory/Planning Performance in Children Born Very Preterm

	Model 1 (F=10.12, p<.001, R^2=.15)			Model 2 (F=9.37, p<.001, R^2=.20)			Model 4 (F=8.49, p<.001, R^2=31)		
	B (SE)	•	p	B (SE)	•	p	B (SE)	•	p
Clinical factor									
Male gender (birth)	-1.83 (0.49)	-0.34	.001	-1.75 (0.49)	-0.32	<.001	-1.66 (0.48)	-0.31	.001
Evidence of infection (birth)	-2.01 (0.71)	-0.26	.01	-1.75 (0.71)	-0.22	.02	-1.45 (0.69)	-0.19	.04
Neurological Factors									
White matter abnormality (term MRI)				-0.31 (.12)	-0.24	.011	-0.16 (0.12)	-0.12	.19
Social Background factors									
Parental changes (0-6 yrs)							-.91 (0.37)	-0.22	.02
Parent-child synchrony (2-4 yrs)							0.91 (0.41)	-0.20	.03

Note. df=99

9.3 Associations between Antecedent Clinical, Neurological and Socio-Familial Factors and Later Executive Attention Performance

Neonatal Clinical Factors Associated with Later Executive Attention Performance in Children Born Very Preterm. Following the identification of these associations between working memory and child and family characteristics, a similar examination of the relationships between these factors and executive attention was completed. Table 9.5 shows the relationships between medical experiences and executive attention composite scores achieved at age 6 years within the group of children born very preterm only. As this factor was made up of a limited number of ordinal rankings, further non-parametric Mann-Whitney U and Kruskil-Wallis tests were conducted after traditional tests in order to confirm findings. The correlations between continuous variables and the executive attention score are shown in Table 1 of Appendix E.

In general, inspection of the relationships between early medical risk and later executive attention suggested that those children who were sickest and least mature tended to experience greater difficulties. Again, male children showed lower levels of executive attention than females ($p<0.001$). Across multiple measures of medical risk, children who had experienced these risk factors tended to obtain lower scores. However, only some of these tendencies reached or approached levels of statistical significance. Specifically, there was a significant relationship with gestation, such that those children who were born at the lowest gestational ages obtained significantly lower scores ($p<0.05$). In addition, there was a tendency for children who had been growth restricted to obtain lower scores, although there were few children in this group, potentially impacting on the power to detect differences ($p=0.08$). Children who had experienced respiratory distress demonstrated poorer performance on the executive attention tasks than children who had not ($p=0.05$), with this tendency also apparent for those cases who had developed chronic lung disease ($p=0.1$). Children with PDA obtained lower scores on executive attention measures ($p<0.05$). Finally, there was a significant relationship with ROP ($p<0.05$), with those children who had developed retinopathy showing lower executive attention scores than their counterparts who had not experienced this clinical condition. Therefore, it was broadly apparent that those children with attentional difficulties at age 6 years were those who had been most medically compromised.

Table 9.5: Relationships between Perinatal Clinical Factors and Executive Attention at Age 6 Years Amongst Children Born Very Preterm

Clinical Factors	N	Mean(SD) Executive Attention Factor Score	F/t	p
Gender				
Male	52	4.67 (1.52)		
Female	49	5.86 (1.49)	3.96	<.001
Gestational age				
23-26 weeks	26	5.00 (1.62)		
27-28 weeks	32	4.81 (1.55)		
29-34 weeks	43	5.72 (1.55)	3.51	0.03
Birthweight				
<750g	17	5.06 (1.39)		
<1000g	25	5.04 (1.51)		
• 1000g	59	5.39 (1.71)	0.55	0.58
Multiple birth				
Twin	34	5.32 (1.79)		
Singleton	67	5.21 (1.52)	0.34	0.74
IUGR				
Yes	11	4.45 (1.51)		
No	90	5.33 (1.65)	1.75	0.08
Maternal smoking during pregnancy				
Yes	39	5.08 (1.53)		
No	61	5.32 (1.66)	0.76	0.45
Maternal antenatal steroids				
Yes	84	5.36 (1.63)		
No	17	4.71 (1.45)	1.53	0.12

Table 9.5: Relationships between Perinatal Clinical Factors and Executive Attention at Age 6 Years Amongst Children Born Very Preterm

Clinical Factors	N	Mean(SD) Executive Attention Factor Score	F/t	p
Maternal chorioamniotis or fever				
Yes	14	5.43 (1.45)		
No	87	5.22 (1.64)	0.45	0.65
Respiratory distress syndrome				
Yes	84	5.01 (1.63)		
No	17	5.94 (1.35)	1.98	0.05
Days of respiratory support (CPAP + IPPV)				
None	7	6.18 (1.63)		
1-10 days	43	5.37 (1.52)		
11-30 days	19	5.06 (1.69)		
30+ days	32	5.03 (1.64)	0.92	0.44
Chronic lung disease				
Yes	34	4.88 (1.55)		
No	67	5.43 (1.62)	1.33	0.10
Patent ductus arteriosis				
Yes	44	4.88 (1.35)		
No	57	5.53 (1.71)	2.01	0.05
Retinopathy of prematurity				
Yes	35	4.80 (1.35)		
No	65	5.49 (1.71)	2.08	0.04

Table 9.5: Relationships between Perinatal Clinical Factors and Executive Attention at Age 6 Years Amongst Children Born Very Preterm

Clinical Factors	N	Mean(SD) Executive Attention Factor Score	F/t	p
Necrotising entercolitis				
Yes	7	4.71 (1.50)		
No	94	5.29 (1.61)	0.91	0.37
Proven sepsis in infant				
Yes	29	5.07 (1.65)		
No	71	5.31 (1.61)	0.67	0.50
Postnatal steroids				
Yes	11	4.82 (1.66)		
No	90	5.30 (1.60)	0.94	0.35

Note. df=99

Neonatal Neurological Factors Associated with Later Executive Attention in Children Born Very Preterm. Following the examination of relationships between early medical risk and later executive attention, neurological factors were considered. As shown in Table 9.6, few relationships between executive attention and measures of neurological integrity reached significance within the very preterm group. Correlations between these neurological factors and later executive attention are also provided in Table 2 of Appendix E. While children with no white matter abnormalities, as rated from MRI scans at term age equivalent, showed a higher average score than those who experienced mild white matter abnormality ($p<0.05$), the relationship between the extent of white matter abnormality and executive attention performance was not linear, with children in the moderate-severe injury group performing at higher levels than those with mild abnormalities. There were no significant relationships between executive attention performance and ultrasound measures of IVH ($p=0.88$) or PVL ($p=0.22$). Inspection of data distributions indicated that the non-linear pattern was not due to outliers. While children with grey matter abnormalities showed lower scores on the executive attention composite, this relationship also did not reach significance ($p=0.58$). These findings were all consistent with those for non-parametric analyses. Thus, in contrast to findings for the executive working memory composite, there was less evidence for a linear relationship between the extent of neonatal white matter abnormality and later executive attention performance amongst children born very preterm.

Table 9.6: Relationships between Term Equivalent Neurological Factors and Executive Attention at Age 6 Years Amongst Children Born Very Preterm

Child Neurological Factors	N	Mean(SD) Executive Attention Factor Score	F/t	p
Severity of IVH (ultrasound)				
No IVH	73	5.23 (1.60)		
Grade I/II IVH	21	5.38 (1.69)		
Grade IV/V IVH	5	5.00 (1.87)	0.13	0.88
PVL (ultrasound)				
Yes	5	4.40 (2.30)		
No	95	5.31 (1.57)	1.44	0.22
White matter abnormality (MRI)				
None (Score <7)	22	6.00 (1.51)		
Mild (7-9)	60	4.92 (1.51)		
Moderate /severe (• 10)	18	5.44 (1.82)	4.02	0.02
Grey matter abnormality (MRI)				
None (Score<5)	42	5.42 (1.56)		
Mild (5-6)	35	5.20 (1.62)		
Moderate/severe (>7)	23	5.00 (1.73)	0.54	0.58

Note. df=99

Socio-Familial Factors Associated with Later Executive Attention Performance in Children Born Very Preterm. Table 9.7 describes the relationships between early measures of social background and family functioning and later executive attention performance amongst children born very preterm. Correlations are also shown in Table

3 of Appendix E. This examination revealed few significant relationships between socio-familial circumstances and executive attention performance at age 6 years. None of the early social background factors considered in these analyses were significantly related to children's ability to regulate their attention at 6 years. However, a significant finding did emerge with regard to early parenting experiences. Specifically, children whose parents had shown more intrusive behaviours during interactions at age 2 and 4 years showed less ability to sustain and flexibly shift their attention at age 6 years ($p<0.01$).

Table 9.7: Relationships between Socio-Familial Factors and Executive Attention at Age 6 Years Amongst Children born Very Preterm

Socio-Familial Factors	N	Mean(SD) Executive Attention Factor Score	F	p
<u>Family background</u>				
Family SES (2/4 years)				
Manual/unemployed	11	5.20 (1.50)		
Semi-skilled/some qualifications	65	5.31 (1.65)		
Professional/managerial	25	5.00 (1.73)	0.18	0.83
Income				
< $NZ 25 000	18	5.00 (1.64)		
• $NZ 25 000	83	5.30 (1.61)	0.72	0.47
Maternal age (term)				
<25 years	11	5.54 (1.81)		
• 25 years	90	5.21 (1.59)	0.65	0.52
Family structure (term)				
Single parent	18	5.39 (1.24)		
Defacto/married	83	5.22 (1.68)	0.41	0.68
<u>Family functioning</u>				
Parental changes (0-6 years)				
No change in parent	72	5.22 (1.66)		
At least one parental change	21	5.24 (1.18)		
>1 change	8	5.50 (2.20)	0.11	0.90
Maternal depression (1-6 yrs)				
None	58	5.16 (1.64)		
At least 1 episode	28	5.50 (1.73)		
>1 episode	14	5.00 (1.18)	0.57	0.55

Table 9.7: Relationships between Socio-Familial Factors and Executive Attention at Age 6 Years Amongst Children born Very Preterm

Socio-Familial Factors	N	Mean(SD) Executive Attention Factor Score	F	p
Maternal anxiety (1-6 years)				
None	52	5.19 (1.56)		
At least 1 episode	25	5.56 (1.81)		
>1 episode	24	5.07 (1.70)	0.69	0.50
Family stress (1-6 yrs)				
Mild stress (<10)	51	5.29 (1.69)		
Moderate stress (10-20)	26	4.96 (1.48)		
High stress (>20)	23	5.43 (1.62)	0.58	0.56
Parenting supportive presence (2 & 4 years)				
Low (1-3)	23	5.09 (1.81)		
Mod (3.5-4)	62	5.19 (1.54)		
High (>4)	14	6.07 (1.27)	2.17	0.11
Parenting intrusiveness (2 & 4 years)				
Low (1)	52	5.73 (1.48)		
Moderate (2-3)	43	4.91 (1.59)		
High (4-5)	14	4.57 (1.60)	4.69	0.01
Parent-child synchrony (2 & 4 years)				
Low (<2.5)	31	5.00 (1.81)		
Mod (2.5-3.5)	52	5.38 (1.59)		
High (>3.5)	17	5.41 (1.23)	0.34	0.53

Note. df=99

9.4 Predictors of Executive Attention in Children Born Very Preterm

Having identified correlations between measures of medical, neurological and socio-familial risk and later executive attention, these factors were entered into a multiple linear regression model to determine which factors were associated with executive attention in the context of multiple correlations. As had been the case for the working memory composite, independent variables were entered in a block recursive fashion, with antecedent clinical factors entered first, neurological factors entered second and measures of family background and function entered last. Where possible, continuous independent variables were used.

The final models are shown in Table 9.7. As can be seen from these models, males obtained significantly lower scores on the executive attention composite than females ($p<0.001$). Similarly, lower gestational age was associated with poorer executive attention at age 6 years ($p<0.05$). When gestational age was included in the model, none of the other measures of clinical risk during the child's course in the NICU were associated with later executive attention.

Consideration of socio-familial factors showed that, in line with findings from univariate analyses, children whose parents had shown higher levels of intrusive behaviour during parent-child problem-solving interactions at age 2 and 4 years, performed less well on these measures of executive attention at age 6 years, although this relationship was at a trend level of significance ($p<0.1$). No other indicators of socio-familial circumstances or functioning were significantly associated with executive attention in this multivariate model. Tests for 2 and 3-way interactions amongst each of these factors were not significant.

Table 9.8: Clinical and Socio-Familial Predictors of Later Executive Attention Performance in Children Born Very Preterm

	Model 1			Model 2		
	(F=10.42, p<001, R^2=.18)			(F=8.30, p<.001, R^2=.21)		
	B (SE)	•	p	B (SE)	•	p
Clinical predictors						
Male gender	-1.17 (.29)	-.37	<.001	-1.10 (.31)	-.34	.001
Gestational age	.13 (.40)	.20	.03	-.89 (.39)	-.21	.03
Family functioning factors						
Parental intrusiveness				-.31 (.17)	-.17	.08

Note. df=98

Collectively, these findings suggest distinct processes underlying difficulties in different facets of executive function amongst children born very preterm. In general, males appeared to be consistently vulnerable to greater impairment across both executive domains by age 6 years. Children who showed difficulties in manipulating information in working memory and in utilising this information during problem solving were more likely to have shown abnormalities in the development of white matter at term age equivalent. In contrast, it seemed that the extent of immaturity and medical fragility were more linearly associated with children's performance on the executive attention factor. Children who showed difficulty in sustaining attention and flexibly applying different strategies during a task with a high requirement of inhibitory control were more likely to have been lower in gestation and to have experienced medical complications such as ROP, IUGR and PDA. It must be noted that mild white matter abnormalities did appear to show some relationship with executive attention, but this relationship was not consistent for children with higher grades of abnormality.

For both of these areas of executive function, family functioning was significantly related to children's performance. Specifically, children who had experienced a higher degree of instability in parenting showed lower performance across measures of working memory and planning. In terms of more proximal processes, the dyadic relationship between the parent and child was clearly important. Children whose parents were less intrusive during early problem solving tasks showed greater abilities across both domains of executive function at age 6 years. For the working memory/planning factor, however, the mutual symmetry between parent and child behaviours was most important when considered in the context of multiple predictors. Clearly, early medical, neurological and social risk factors each play a role in the development of children's executive functioning and attentional regulation. The implications of these executive impairments for children's functioning during their transition to the classroom will be discussed in the following chapter.

Chapter 10

Results 5: Associations between Executive Function and Early Academic Achievement in Children Born Very Preterm and Full Term

A major focus of preceding chapters has been the description of the profile of executive function in children born very preterm. If these results are to inform us about where best to direct intervention efforts, it is important to establish the ecological validity of the executive function measures beyond an artificial laboratory setting. Although the causal direction of the relationship between executive impairments and academic achievement cannot be determined from this study, background literature highlights the importance of effective executive skills for achievement in key academic areas such as mathematics and language comprehension (Blair & Razza, 2007; Bull & Scerif, 2001; D'Amico & Guarnela, 2005; Gathercole et al., 2005; Jeffries & Everatt, 2004). As children transition to the school environment, working memory, planning and executive attention skills will increasingly be taxed in learning, behavioural and social domains. It seems likely that the demonstrated impairments in executive function in many of the children born very preterm will have ongoing repercussions for the development of key academic skills.

In support of this, chapter 6 showed that children born very preterm achieved lower scores on standardised measures of mathematics and receptive language achievement. Furthermore, teachers of children born very preterm were more likely to report delays in mathematics, reading and receptive language than those of children born full term. Given these group differences in both executive and academic domains, the third aim of this study was to examine the links between composite executive function scores and achievement in mathematics, reading and language comprehension at age 6 years. Particular emphasis was placed on determining the added utility of executive function measures in accounting for group differences in achievement over and above a traditional measure of IQ.

In order to address these aims, both the full term and very preterm groups were included in the analyses. First, associations between the composite measures of executive function and measures of academic achievement were examined for each group. Associations between academic achievement and a number of covariate factors were also considered. Potential covariates included child neurodevelopmental characteristics, such as general cognitive performance (IQ), cerebral palsy and corrected vision. Socio economic discrepancies between the groups were also taken into account, as the availability of economic resources is a well-established correlate of academic achievement (Johnson et al., 2007; Walker et al., 2005). These descriptive analyses allowed for an examination of the extent of overlap between these different factors, thereby assisting in the selection of relevant covariates for the next set of analyses. During this next phase, a series of multivariate models were constructed in order to determine the relationship between gestation group and achievement once individual differences in executive function had been accounted for. These models also considered the influence of identified covariates, in order to assess the added value of information on executive function in predicting academic achievement over and above these other, more widely used markers of developmental risk.

10.1. Associations between Working Memory/Planning Performance and Academic Achievement

Table 10.1 reports the associations between measures of academic achievement and the working memory factor across 1) the very preterm and 2) the full term group. For illustrative purposes, children were divided into groups according to their performance score on the measure of working memory (<8= low, 8-12 = medium, >12 = high). Standardised measures of academic achievement include the Woodcock-Johnson Passage Comprehension measure, the Woodcock-Johnson Maths Fluency measure, and the Woodcock-Johnson Understanding Directions measure. Associations between working memory/ planning performance and dichotomous teacher ratings of achievement in reading, arithmetic and language comprehension are also included in the table. Additionally, the p-values for the effect of working memory score (low, medium or high) and the interactions between group status and working memory scores are presented in this table, based on the results of univariate ANOVAs and logistic regression analyses. Correlations between continuous executive function scores and measures of academic achievement are also provided in Table 4 of Appendix E.

As shown in Table 10.1, lower performance on the working memory/planning factor was associated with lower academic achievement scores for both groups of children ($p<0.001$). There were no interactions between working memory and gestation group. This pattern was replicated when teacher ratings, rather than standardised tests of academic achievement were examined. Children who achieved lower scores on the measure of working memory/planning were more likely to be rated by their teachers as delayed or below average in reading, mathematics and language comprehension ($p<0.05$). This pattern was generally consistent across both groups of children, with no interactions between very preterm birth status and working memory/planning scores.

Collectively, findings in Table 10.1 reveal robust associations between children’s ability to plan and utilise working memory and their ability to perform basic mathematics, reading and receptive language tasks, with this relationship being consistent across both groups of children. Thus, while children in the preterm group showed were more likely to show evidence of executive planning/working memory impairment, children in the full term group who had these difficulties were also likely to show poorer academic functioning.

Table 10.1: Associations between on Working Memory/Planning Performance and Academic Achievement in Children Born Very Preterm and Full Term at Age 6 Years

	Working Memory/plan score							
	Preterm			Full Term				
Achievement Measure	Low (n=28)	Average (n=53)	High (n=20)	Low (n=15)	Average (n=58)	High (n=35)	p[a]	p[b]
Reading								
M (SD) Passage Comprehension	100.00 (11.56)	109.62 (15.72)	121.00 (9.87)	98.67 (14.32)	111.79 (14.34)	121.14 (12.87)	<.001	.77
% Below average/ delayed[c]	82.1	45.8	11.1	66.7	21.8	11.4	<.001	.52
Mathematics								
M (SD) Maths Fluency	88.82 (5.21)	97.62 (6.63)	99.20 (8.35)	93.60 (7.21)	101.31 (7.36)	108.14 (6.04)	<.001	.08
% Below average/ delayed	75.0	37.5	16.7	57.1	35.7	2.9	<.001	.25
Receptive language								
M (SD) Understanding Directions score	104.19 (10.08)	111.09 (7.96)	113.90 (7.50)	105.86 (7.38)	112.38 (7.68)	118.34 (5.01)	<.001	.47
% Below average/ delayed	53.6	25.0	16.7	33.3	12.7	8.6	.001	.35

[a] Effect of working memory/planning group; [b] Gestation group*working memory group; [c]Rated by classroom teacher

10.2. Associations between Executive Attention Performance and Academic Achievement

Table 10.2 describes the associations between children's performance on the composite measure of executive attention and their performance on the academic achievement tasks. Again, children were divided into achievement groups based on the score they had obtained on the executive attention composite (low = <4, medium = 4-6, high= >6). Consistent with findings for the working memory and planning tasks, there were significant associations between children's performance on measures of executive attention and all standardised measures of academic achievement administered in the laboratory ($p<0.01$). Similarly, within the very preterm group, children showing poor executive attention scores were more likely to be rated as delayed or below average by their teachers across all of the achievement domains assessed ($p<0.01$). The positive predictive value of a low executive attention score was particularly evident in reading, where 94% of children who had achieved low scores on the attention composite were also rated by teachers as performing poorly in this domain. Relationships were less clear in the full term group. Children who achieved average scores on the executive attention composite were equally as likely as those who had achieved poor scores to be rated by teachers as performing below average in reading and language comprehension, although none of the tests for interactions reached statistical significance.

Together, these analyses suggest that there are strong relationships between children's ability to plan and manage goal-directed behaviour, manipulate information in working memory and flexibly attend to relevant stimuli, and their performance in key academic domains, as measured from two independent sources. The greater prevalence of both executive impairments and academic difficulties in the group of children born very preterm raises the question of whether discrepancies in the performance of the preterm group on measures of academic achievement may be mediated by poor executive function.

However, correlations (shown in Table 4 of Appendix E) also suggested clear associations between children's neurodevelopmental functioning and academic achievement. As expected, with decreasing general cognitive performance (IQ) scores, children performed less well on the executive function and academic achievement measures (r =.31-.63, $p<0.001$). Similarly, with increasing severity of CP, children in the very preterm group tended to perform more poorly on the working memory/planning factor and measures of academic achievement (r_s = -.22 - -.34, $p<0.01$). Finally, across the whole sample, children who were wearing glasses by age 6 years also tended to demonstrate lower performance on both measures of executive function and measures of achievement (r_s =-.18 - .27, $p<0.01$). Given that children born very preterm are also at increased risk of these neurodevelopmental impairments, this raises a second question as to whether measures of executive function are able to explain any more group variance in academic achievement than what is already explained by these more traditional measures.

Table 10.2: Associations between Executive Attention Performance and Academic Achievement Among Children born Very Preterm and Full Term at Age 6 Years

	Executive Attention Score							
	Very Preterm			Full Term				
Achievement Measure	Low (n=18)	Average (n=34)	High (n=47)	Low (n=6)	Average (n=18)	High (n=84)	p[a]	p[b]
Reading								
M (SD) Passage Comprehension	100.94 (12.74)	111.82 (15.59)	111.09 (15.12)	99.00 (16.04)	107.78 (17.52)	115.12 (14.38)	<.001	.26
% Below average/ delayed[c]	94.1	39.4	39.5	33.3	50.0	18.5	<.001	.70
Mathematics								
M (SD) Maths Fluency	90.66 (5.35)	96.09 (8.44)	97.13 (7.42)	91.67 (5.82)	99.17 (7.51)	103.93 (7.94)	<.001	.17
% Below average/ delayed	82.4	33.3	37.2	50.0	38.9	5.00	<.001	.08
Receptive language								
M (SD) Understanding Directions	103.59 (9.78)	108.71 (7.94)	113.49 (7.42)	101.67 (9.93)	108.00 (7.29)	115.48 (7.91)	<.001	.42
% Below average/ delayed	64.7	24.2	25.6	16.7	38.9	8.6	.003	.74

[a] Effect of working memory/planning group; [b] Gestation group*working memory group; [c]Rated by classroom teacher;

10.3 Multivariate Associations between Executive Function and Academic Achievement in Children born Very Preterm and Full Term

To assess whether individual differences in executive function might explain relationships between very preterm birth and academic achievement on the Woodcock-Johnson Maths Fluency and Passage Comprehension subtests, a series of linear regression analyses were performed. In each regression model, a dummy variable, discriminating children born very preterm from those born full term, was entered first. A simple model including 1) the working memory/planning measure and 2) the executive attention measure was run to determine the extent to which the association between birth status and academic achievement was attenuated by the inclusion of each executive function measure. Mediational analyses were conducted in accordance with guidelines of Baron and Kenny (Baron & Kenny, 1986). Sobel's tests were performed to determine whether the indirect effect of the independent variable (gestation group) via the posited mediator (executive function) was significantly different from zero (Baron & Kenny, 1986; Preacher & Hayes, 2004) [2]. Group differences on the Passage Comprehension subtest from the Woodcock-Johnson Achievement battery were not significant after controlling for differences in socioeconomic status.

To address the issue of whether the measures of executive function explained more group variance than other traditionally recognised covariates, the original models were extended to include family SES, general cognitive ability (IQ), severity of cerebral palsy and corrected vision (glasses). Covariates that were significant were retained in these

[2] The formula for the Sobel's test is ab/s_{ab}. $s_{ab} = \sqrt{b^2 s_a^2 + a^2 s_b^2 + s_a^2 s_b^2}$, where a = the regression coefficient for the path from the independent variable to the mediator, b= the regression coefficient for the path from the mediator to the dependent variable and s_a and s_b are the standard errors for each of these paths. ab= the regression coefficient of the independent variable prior to adjustment for the mediator – the regression

models.

10.3.1 Associations between Executive Function and Mathematics Achievement in Children Born Very Preterm and Full Term

Figure 10.1 depicts a model of the relationship between working memory and achievement on the Woodcock-Johnson measure of Maths Fluency. Children who were unable to complete any of the items correctly (n=24) were allocated a score of 85, the lowest possible score on this measure for this age group. The initial regression model showed that gestation group was significantly associated with the maths fluency score, confirming between-group differences in performance ($p<0.001$). This direct association is described in pathway A of Figure 10.1. The pathway shows the unstandardised (B) and standardised (•) regression weights, standard error (SE) and levels of significance (p) for group status prior to the consideration of working memory performance. With the addition of the working memory composite score, the impact of gestation group on mathematics achievement continued to be significant, B (SE) = 4.43 (0.97), $p<0.01$. However, a Sobel's test confirmed a significant reduction in the association between birth status and maths fluency ($z = 3.64$, $p<0.01$). The indirect effect of gestation group after the consideration of working memory is shown in path C of the model. These findings suggest that the impact of very preterm birth on mathematics ability may be partially accounted for by group differences in the ability to plan, strategise, and hold and sequence information in working memory.

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coefficient after adjustment for the mediator.

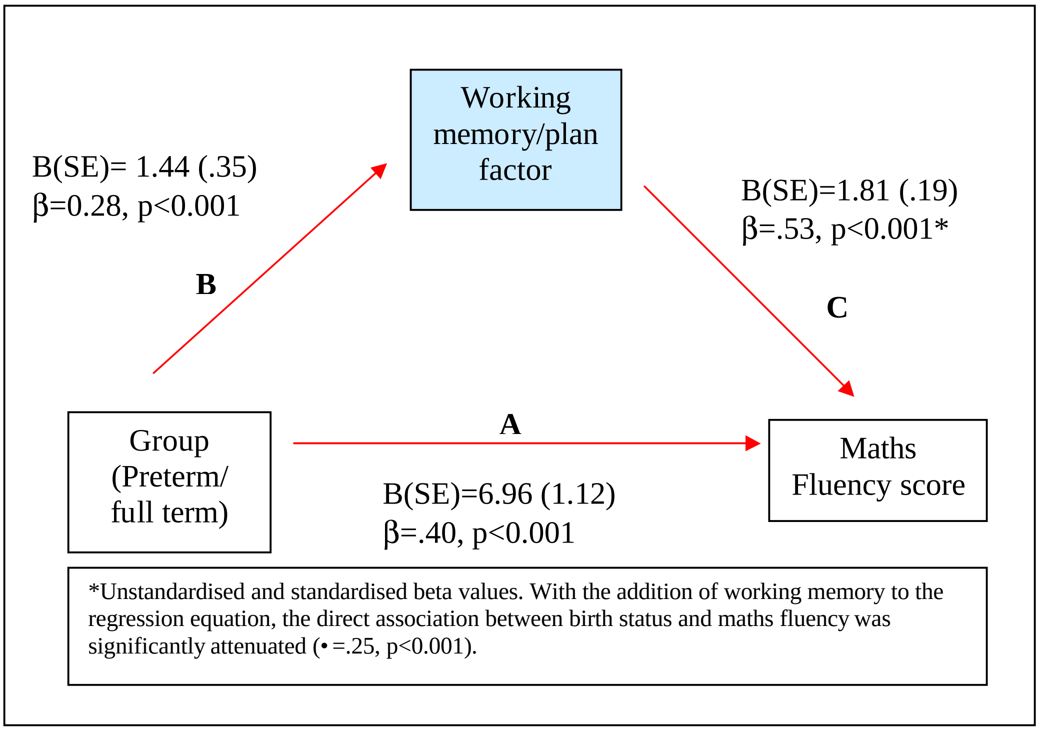

Figure 10.1: Model of the Effect of Working Memory on the Relationship between Very Preterm Birth and Mathematics Achievement

Figure 10.2 describes a similar regression model completed with the executive attention factor as an independent variable. With the addition of children’s executive attention scores to a model including birth status group, there was a significant attenuation in the relationship between gestational group and maths fluency. However, the effect of group remained significant in predicting mathematics performance scores, B(SE) = 4.77 (1.14), $p<0.001$. In order to determine whether the additional consideration of attentional control accounted for associations between very preterm birth status and mathematics achievement, a Sobel’s test statistic was calculated. This test indicated that the addition of the executive attention factor to the regression model significantly attenuated the effect of group status, indicating partial mediation of maths fluency by executive attention ($z=3.78$, $p<0.001$).

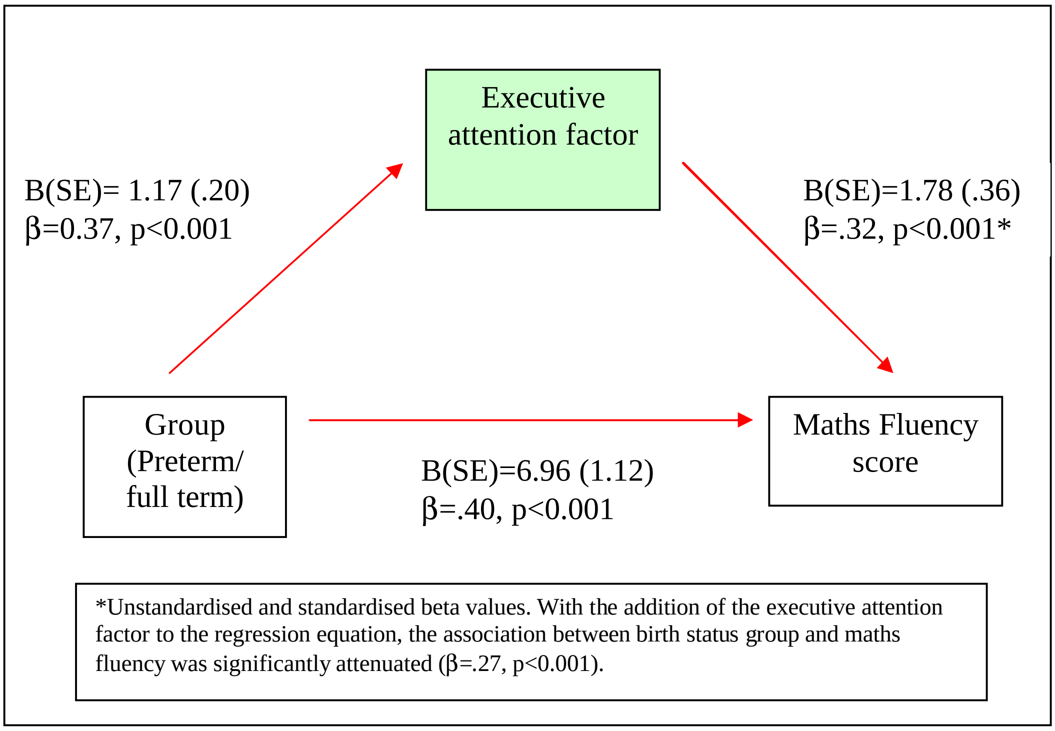

Figure 10.2: Model of the Effect of Executive Attention on the Relationship between Very Preterm Birth and Mathematics Achievement

However, these models do not account for covariates. In order to assess whether there were significant associations between the composite executive scores and achievement after group differences in SES and neurodevelopmental factors (IQ, severity of CP and corrected vision) were accounted for, the multivariate models were extended to include these variables. The results of these models are shown in Table 10.3. As can be seen from this table, after the inclusion of IQ, no other covariates were significant. However, working memory/planning performance continued to be associated with children's performance on measures of mathematics achievement ($p<0.001$) independent of general cognitive performance, suggesting predictive utility of this measure independent of what one would gain from the consideration of IQ alone. In contrast, the executive attention composite scores were no longer significantly associated with Maths

Fluency scores (p=0.23).

Table 10.3: Relationships between Executive Function and Mathematics Achievement after Adjustment for Covariates

	Model 1 (F=69.36, p<0.001, R^2=.51)			Model 2 (F=56.03, p<0.001, R^2=.44)		
	B (SE)	β	p	B (SE)	β	p
Very preterm birth	2.67 (.94)	0.15	0.005	2.46 (1.00)	.14	.02
Working memory composite	0.10 (.22)	.57	<.001			
Executive attention composite				.41 (.34)	.07	.23
WPPSI IQ	.25 (.04)	.41	<.001	.35 (.04)	.57	<.001

Note. df=206

Together, these analyses of the relationships between executive function and children's mathematics achievement show that variation in executive function performance explained a substantial amount of the variation in mathematics achievement between the very preterm and full term groups of children. However, when covariates, and children's general cognitive ability in particular, were considered, only working memory/planning performance continued to be associated with mathematics achievement.

10.3.2 Associations between Executive Function and Receptive Language Achievement in Children Born Very Preterm and Full Term

A similar set of analyses was performed with the total Woodcock-Johnson Understanding Directions score as the dependent variable. A model of the relationship between gestation group, Understanding Directions and the working memory/planning factor is illustrated in Figure 10.3. As can be seen from pathway A of the model, an initial regression analysis confirmed that very preterm birth was associated with lower scores on this measure ($p=0.003$). However, with the introduction of the working memory/planning composite (pathway C) to the model, this association became non-significant ($p=0.30$). A Sobel's test indicated a significant reduction in the effect of group on the Understanding Directions score after the addition of the working memory/planning composite score ($z = 3.74$, $p<0.001$).

Figure 10.4 depicts findings from a regression model including birth status and executive attention. As this figure shows, the introduction of the executive attention composite score caused the relationship between gestational age group and Understanding Directions to become non-significant ($p=0.70$). A Sobel's test indicated that the reduction of the association between gestation group and Understanding Directions score was statistically significant ($z= 4.62$, $p<0.001$).

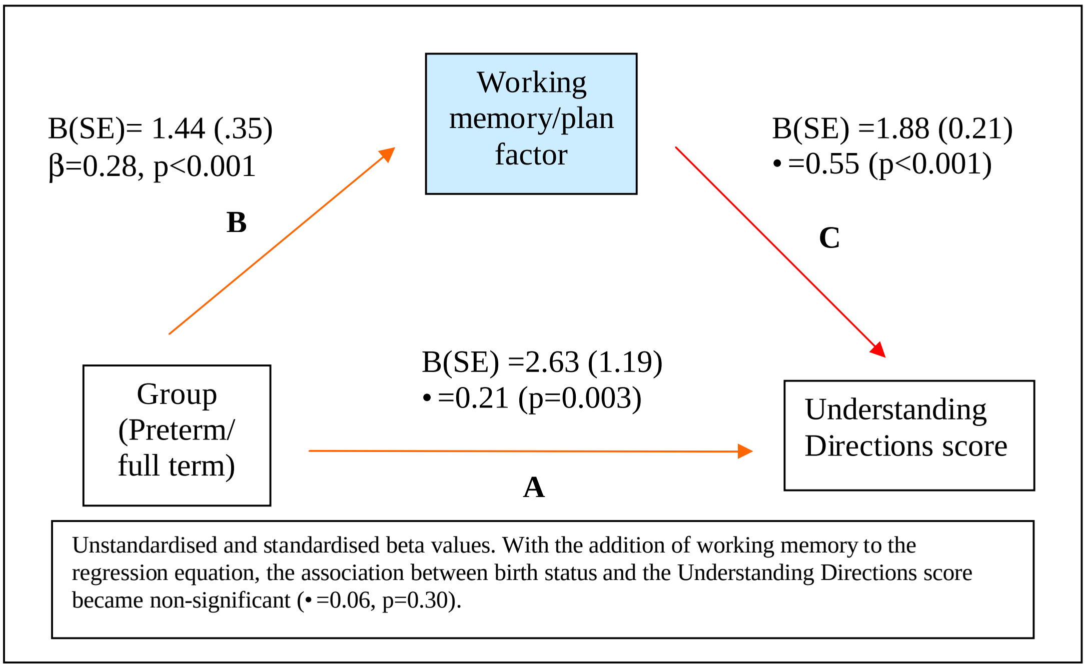

Figure 10.3: Model of the Effect of Working Memory/Planning on the Relationship between Very Preterm Birth and Receptive Language Achievement

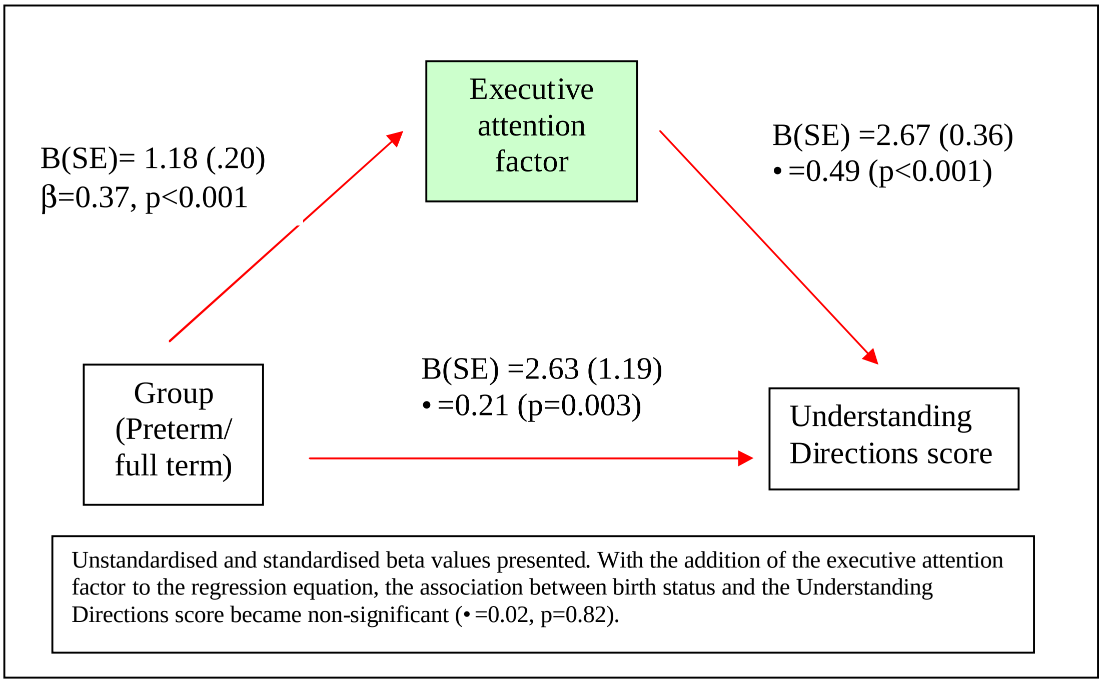

Figure 10.4: Model of the Effect of Executive Attention on the Relationship between Very Preterm Birth and Receptive Language Achievement

These findings suggest that executive functions play an important role in the ability to recall and respond to a series of directions. However, it is also important to establish whether measures of executive function are able to offer any more information about children's receptive language performance than traditional measures of neurodevelopmental impairment. In order to assess this, the former analyses were extended to included covariates that were associated with children's performance on the Understanding Directions subtest. The results of these models are shown in Table 10.4. As can be seen from these models, children's general cognitive performance scores and family SES were significantly associated with between-group differences on the measure of language comprehension. After consideration of these covariates, the effect of birth status was diminished so that it was no longer significant ($p=0.19$). However, both working memory/planning performance and executive attention performance continued to be associated with individual differences in performance on this measure ($p<0.001$), suggesting that difficulties in the ability to sustain attention, flexibly attend to rules, plan and utilise working memory may help to account for the poor performance of children born very preterm on a measure of complex language comprehension.

Table 10.4: Relationships between Executive Function and Receptive Language Achievement after Adjustment for Covariates

	Model 1 (F=37.73, p<.001, R²=.44)			Model 2 (F=37.58, p<0.001, R²=.44)		
	B (SE)	β	P	B (SE)	β	p
Very preterm birth	-1.33 (1.00)	-.08	.19	-2.36 (1.00)	-.14	.02
Working memory composite	.91 (.23)	.27	<.001			
Executive attention composite				1.68 (.34)	.32	<.001
Family SES	-.85 (.31)	-.15	.007	-1.00 (.31)	-.18	.001
IQ	.27 (.04)	.44	<.001	.28 (.04)	.46	<.001

Note. df=198

Collectively, these findings suggest that the knowledge that a child born very preterm has difficulty in executive function can help to inform us about their risk for academic achievement difficulties at early school age, supporting the ecological validity of these measures. While the direction of the relationship between executive function and achievement cannot be determined, a theoretical model, supported by literature on the relationship between executive function and school achievement in typical groups of children, suggests that difficulties in these domains within the very preterm group may be affecting the ability to achieve in a classroom environment. Tests for the mediation of very preterm birth status by executive function showed that this is a plausible model, with consideration of the executive function measures significantly attenuating relationships between preterm birth status and achievement in each academic domain. Despite the substantial overlap between measures of executive function and measures of general cognition, they continued to be associated with academic performance after adjusting for IQ, highlighting added utility of these measures over and above information gained from traditional testing.

Chapter 11

Discussion

11.1 Overview of Study Findings

As a consequence of improved neonatal medicine and technology, increasing numbers of children born extremely preterm and very preterm will make the transition to school. Extensive follow-up studies have clearly established that these children are at risk for later cognitive, behavioural and academic impairments. Such difficulties will have ongoing impacts, both at macro-social levels of educational service use, resourcing and growing economic costs, and also at micro-social levels, including growing pressure on teachers and stress for families and children themselves. Detailed research into the early developmental processes and mechanisms that may result in lower achievement for children born very preterm is essential if we are to help to lessen the difficulty of their transition to the demanding school environment and ensure a high quality of life for these children and their families.

This study examined the early profile of executive function in a large, regionally representative sample of children who were born very preterm and/or VLBW and who had recently made this transition to primary school. Methodological strengths of this study were numerous. Strengths included high recruitment and retention rates and multiple informants across different ecological settings. Children were matched for adjusted age to a group of full term control children, helping to minimise a reliance on norms that were potentially outdated or that were not applicable to international samples. Added to this, the prospective, longitudinal nature of the study afforded a detailed developmental history of children and families. In contrast to previous studies, which have generally relied on ultrasound or proxy measures of neurological risk (e.g. Luciana et al., 1999; Taylor et al., 2006), this is the first study to examine longitudinal relationships between early measures of brain abnormality detected by advanced MR imaging and a comprehensive set of executive function measures in preterm children of early school age. Finally, the incorporation of both traditional, standardised measures and more novel, complex tasks allowed for the evaluation of a range of specific cognitive abilities and problem-solving strategies. Findings related to each of the study aims are discussed below.

11.1.1 Cognitive and Academic Performance of Children born Very Preterm and Full Term at Age 6 Years

The first part of this study involved the comparison of performance of children born very preterm and full term on standardised measures of IQ and academic achievement. The distribution of IQ scores obtained by children born very preterm in Christchurch was similar to other cohorts reported in international studies (Bhutta et al., 2002; Saigal et al., 2000). In relation to their full term peers, children in the very preterm group obtained lower scores across all IQ subtests administered. The average IQ of children in the very preterm group was 12 points below those born full term, despite the fact that children in the very preterm group were advantaged by scoring based on corrected gestational age. Children in the very preterm group also showed a higher standard deviation in their scores on the IQ test, suggesting a greater variability in performance. In addition, children born very preterm were more likely to show severe and mild cognitive impairments, defined as scores one or two standard deviations below the normative mean. While their IQ scores were suppressed as a group, most children born very preterm achieved scores within the average range. Nonetheless, the average IQ difference equates to a large effect size (0.88) and will indubitably have implications for the learning and achievement of these children.

Also of interest, the mean cognitive score for the full term group in this study was approximately 106, with the majority of children in this group achieving scores above 100. Such findings are also consistent with recent international literature, which shows that mean IQ scores in full-term control groups are generally higher than the standardised norm of 100, ranging from 102 to 113 (Breslau et al., 2001; McGrath & Sullivan, 2002; Rickards et al., 2001; Short et al., 2003; Sykes et al., 1997). These differences may reflect the Flynn effect, which has been shown to result in an increase of approximately 3 IQ points for every decade of use of an IQ test (Kanaya & Ceci, 2007). Such discrepancies in the standardised mean scores and the scores of control groups highlight the importance of having a representative full term group with which to compare the performance of children born very preterm.

While children in the very preterm group did show lower global performance scores on the measure of IQ, examination of the effect sizes for each of the administered subtests provides some indication that tests taxing fluid intellectual processes, such as reasoning and flexible problem-solving, may pose more of a challenge than tests requiring more crystallised, learned forms of knowledge. This is demonstrated by the fact that effect sizes were greater for tests that placed high demands on the ability to manipulate information in working memory (i.e. block design and arithmetic). While the restricted range of subtests employed in this study curtails any extrapolation of these results, findings do highlight the need to perhaps examine fluid cognitive skills in more detail.

Findings also showed that children in the very preterm group achieved lower mean scores across all of the standardised academic achievement measures, including Passage Comprehension, Maths Fluency and Understanding Directions, than children born full term. However, the group difference for the measure of reading (Passage Comprehension) did not reach statistical significance, with both groups of children achieving high scores on this subtest, relative to the standardised norm (100). Group differences were most evident in mathematics performance. Approximately 20% of children in the very preterm group were unable to complete any of the addition/subtraction problems administered correctly, compared to only 5% of full term children. Added to this, there was a significant difference in overall scores across the two study groups amongst those children who were able to complete at least one of the problems administered.

The evidence for a greater between-group discrepancy in mathematics is consistent with findings from international studies. It appears that children born at extremely low birth weight and children who have global cognitive deficits are likely to show a diffuse pattern of achievement difficulties, including difficulties in reading and language-based skills (Breslau et al., 2001; Grunau et al., 2002; Saigal et al., 2000). However, mathematics has consistently been highlighted as an area of particular difficulty for children born very preterm/VLBW, even in the absence of more severe intellectual impairment (Breslau et al., 2001; Breslau et al., 2004; Hack et al., 1992; Isaacs, Edmonds, & Gadian, 2001; Litt et al., 2005).

Another interesting finding related to the standardised achievement data is that children born very preterm performed less well on the receptive language measure, which required children to point to a series of pictures based on complex sequences of verbal instructions. Again, this finding persisted after children with low IQ scores were excluded from analyses. To date, studies of the language development of children born very preterm have yielded somewhat inconsistent results, with differences in performance often attenuated when general cognitive impairment is taken into account (Aram, Hack, Hawkins, Weissman, & Borawski-Clark, 1991; Gallagher & Watkin, 1998; Seidman, Allen, & Wasserman, 2986). However, this particular receptive language test placed a substantial load on the retention and manipulation of information in working memory. In a classroom environment, understanding and responding to complex sequences of verbal instructions is undoubtedly of great importance. Similarly, difficulties in complex language processing may have implications for interactions with peers and are likely to create more difficulty as academic tasks grow more difficult and children are expected to integrate and interpret several pieces of information.

In support of the ecological validity of laboratory-based achievement measures, further analyses indicated that academic difficulties were also evident in the classroom. When asked to report on the performance of children born very preterm in relation to their classroom peers, teachers rated children born very preterm as being twice as likely to be functioning at a level below average in reading. In mathematics, children born very preterm were three times more likely to be performing below average. Children in the very preterm group were also twice as likely to be rated by teachers as being below average in their ability to comprehend language. Thus, the difficulties reported on tests administered in the laboratory are clearly evident to teachers in the classroom environment, even at this early age.

One important question regarding these findings was whether differences in achievement and cognitive performance seen in the very preterm group arose in part due to the lower SES of families in the very preterm group. The association of very preterm birth with more impoverished environmental circumstances sets up a natural protocol for the observation of complex interactions between nature and nurture. Following statistical adjustment for the effects of SES, between-group differences did not attenuate differences in performance between these groups for IQ or mathematics. However, for achievement tests involving language-based skills, there was some indication that SES did have an impact on individual performance. When the group differences in SES were considered, between-group differences on the standardised test of reading were clearly attenuated. In contrast, performance on the receptive language measure was associated with both SES and very preterm birth status, suggesting that there may be an additive impact of these factors on children's language development.

It must be acknowledged in the interpretation of the achievement test findings that this is a very early age for identification of learning difficulties. There is the possibility that these children had not yet been taught skills or that different schools placed varying emphasis on reading and mathematics. For example, a few children from each study group were attending schools with alternative teaching philosophies (e.g. Rudolf Steiner), in which the teaching curriculum does not emphasise the early development of reading or mathematics. These children may have been disadvantaged by the focus on these domains. However, this is unlikely to have impacted on all between-group differences because the use of a teacher questionnaire also indicated a greater prevalence of delay or difficulty in these learning domains when children born very preterm were compared to their class peers. This classroom-based comparison largely circumvents any confounding issues regarding differences in schooling.

Group discrepancies at this early age raise important concerns because key reading and mathematical skills that are taught at school entry serve as the foundation for subsequent concepts and learning. As other children master basic concepts, such as addition and subtraction, they are likely to move ahead more quickly, setting up a different learning trajectory. This phenomenon is known as the “Matthew effect” (Wood, 1998). Early difficulties in learning may also have an impact on children’s motivation and self-esteem, further undermining effort and achievement in subsequent years. It is therefore unlikely that these early difficulties will become less apparent as children mature. Indeed, the presence of difficulties at this very early age suggests an urgent need for information as to their genesis and development.

Collectively, findings from the first results section of this thesis suggest that this sample of children born very preterm showed a similar cognitive profile to samples reported in other studies, with generalised difficulties across cognitive domains evident, as well as some evidence of more specific impairments. In terms of their achievement in the classroom, children in the very preterm group also showed evidence of impairment, with difficulties being especially prevalent in the area of mathematics.

11.1.2 Executive Function of Children Born Very Preterm at Age 6 Years

Following the description of more general cognitive and achievement difficulties in children born very preterm, this study explored specific cognitive skills in an effort to better understand the difficulties that may be contributing to global between-group differences in achievement. The neuropsychological measures employed for this purpose included a series of novel tasks identified as being suitable for use with 6 year old children and tapping new or emerging executive function skills. While they are not standardised, there is a large theoretical background supporting the sensitivity of these measures to neurological insult or disorder (Denckla, 1996; Fischer, 2001; Gathercole et al., 2004; Gioia et al., 2001; Hughes & Russell, 1993; Inder et al., 2003; Lezak et al., 2004), suggesting potential utility of these measures for the detection of specific neuropsychological deficits in early school aged children.

Working Memory. The first measures employed were selected to tap children's ability to store and manipulate information in working memory. Groups did not differ in forward Digit Span once SES differences between the groups were statistically taken into account. Such findings may indicate that the phonological processing of sequential information is not a specific challenge for children born very preterm. However, some indication of group differences on the Digit Span measure did emerge when children were required to recall digits in reverse order. Although children in the very preterm group showed similar span levels to their full term peers, they were less likely to show consistent performance. This is indicated by the fact that they passed fewer trials overall. It has been recommended that a consideration of both span length and number of trials passed is beneficial for Digit Span measures because of the restricted range in span that individuals are able to achieve (Lezak et al., 2004). Generally, backward span levels across both study groups were low (2-4), suggesting possible floor effects on this measure. Thus, consideration of the overall number of trials passed potentially provides a more accurate representation of performance.

Added to these findings, children in the very preterm group were less likely to be able to pass the first, 2-digit trials of the backward span test, suggesting a lack of understanding of the requirements of this phase of the task or an inability to reverse the numbers at all. Indeed, observations during testing showed that these children would continue to repeat the digits in forward sequence as opposed to reversing them, despite repeated explanations and demonstrations. Although this limitation was not anticipated in piloting of the measures, previous researchers have also observed this problem (Sansavini et al., 2007). Indeed, Sansavini et al. (2007) found that being unable to complete span tasks was associated with poorer expressive language outcomes in young children born very preterm. Therefore, although group differences in span levels were not statistically significant when children who could not complete criterion trials were excluded from analysis in the current study, further consideration of achievement on the backwards Digit Span task was deemed appropriate, given the robust discrepancy in the number of children able to pass initial trials.

In terms of the measure of spatial working memory (the Corsi Blocks), group differences in performance were only apparent for the backwards phases of the task. The effect size for the group difference in backward span was larger for spatial than for Digit Span trials. Interpretation of findings for the Corsi Blocks task is difficult, given that relatively little research has used this task with children, studies attempting to elucidate the specific mechanisms involved in task performance for adults have produced conflicting results and few studies have examined both forward and backward performance (Berch et al., 1998; Vandierendonck, Kemps, Fastame, & Szmalec, 2004). However, one study may be of particular relevance to findings of this thesis. Mammarella and Cornoldi (2005) found that children with a diagnosis of visuo-spatial learning disability did not perform poorly in comparison with matched controls on the forward span trials of the Corsi Block Task. Additionally, children with visuo-spatial disabilities did not perform more poorly on the forward or backward Digit Span task, suggesting that their difficulties were not with backward sequencing per se. However, they performed less well on the backward trials of the Corsi Block task. Based on these results, the researchers argue that the backward span task relies less on sequential processing and more on non-sequential visuo-spatial working memory processes. Therefore, children with visuo-spatial difficulties are able to compensate for their lack of visuo-spatial skills via preserved sequencing in the forward trials. Similarities in the profile of difficulties reported by the above study and the very preterm group included in the current study may indicate a correspondence between very preterm birth and specific visuo-spatial impairments.

Collectively, it is clear that children in the very preterm group showed greater discrepancies on the backward span phases of the verbal and spatial working memory tasks, with impairments being more pronounced on the spatial working memory measure. Perhaps the most plausible explanation for the impaired performance of children born very preterm on the backward span trials of both the verbal and spatial memory tasks is that these trials have an added requirement to reverse the order of output. In order to do this, children may need to employ different strategies to those used for forward sequencing, with the likelihood being that these tasks place a greater burden on central executive resources (Lezak et al., 2004). The extended simultaneous processing requirements of these measures may overwhelm the working memory capacity of children born very preterm. These findings support the notion that short term memory per se may not be an area of specific difficulty for these children. Instead, extended demands on executive resources result in decreased performance on cognitive tasks.

Findings for the working memory measures are very much in keeping with research concerning executive function in children born very preterm. As outlined in the introduction, preschool-aged children born very preterm have been shown to perform less well on tasks that involve remembering the locations of objects, in comparison to their full term peers (Espy et al., 2002; Ross, Lipper et al., 1996; Woodward, 2005). In older children born very preterm, difficulties have also been found with tasks that involve memory for patterns and designs (Isaacs et al., 2000) and with spatial sequencing tasks similar to the one employed in this study (Bohm et al., 2004; Curtis et al., 2002; Kulseng et al., 2006; Taylor et al., 2004). Where the results for these tasks have been probed further, differences between the performance of children born very preterm and full term appear to be more pronounced for items that place more substantial demands on working memory resources, in terms of the number of items children are required to remember, as well as the time over which they are required to remember information (Curtis et al., 2002; Vicari et al., 2004).

Nonetheless, one limitation that is common to these span tasks is that they may tap a number of other processes. For instance, although the Digit Span task was selected from the working memory composite of the WISC and several researchers have used it to assess working memory (Gathercole et al., 2004; Jeffries & Everatt, 2004), it is also often referred to as a measure of attention (Meltzer & Krishman, 2007). The division of this task into forward and backward components may have helped to combat this in that children in the very preterm group did not show difficulties on forward trials, helping to control for differences in underlying processing and attention skills. However, these tasks were not counterbalanced, in that backwards trials for both tasks were always administered after forwards trials. This means that there may have been differences in sustained attention, with children who had shown good performance in beginning trials gradually losing attention. In addition, there may have been some impact of proactive interference as the task progressed. Specifically, former memory traces for sequences of digits may have interfered with the retention and recall of subsequent information.

Other researchers have suggested that span tasks do not place as substantial a burden on working memory as tasks that require simultaneous storage and calculation or utilisation of information. Therefore, counting span and sentence span tasks, requiring children to continuously update information for current tasks with information from previous span levels, are often used in executive function research (Daneman & Merikle, 1996). These may be useful measures to employ in future assessments of this cohort. However, given that several children in the current study were unable to understand instructions for these more simple span tasks, it is unlikely that more complex tasks would have been developmentally appropriate. Indeed, the discrepancies found on the current, more simple span tasks, suggest that they are sensitive indicators of difficulty, at least in this young age group.

Planning/problem Solving. A second area of executive function that this study examined was planning and problem solving. In order to measure this construct, a widely used measure of planning, the Tower of Hanoi, was used. Findings from this study showed that children born very preterm were less likely to be able to complete the 2-move level of the Tower of Hanoi task, which required children to follow three task-related rules. In general, the performance profile on this task was similar to that for IQ scores. The distribution in the very preterm group appeared to peak lower than that of the full term group and fewer children in the very preterm group reached higher levels of the task.

Closer consideration of the cognitive demands of this task suggests that as children progress through the levels, the demands on executive function become greater. For example, the 2-move level of the task required children to understand and abide by three simple rules. Despite demonstrating a verbal understanding of these rules, which was a requirement for commencement of the task, several children showed a tendency to break them. This is similar to the dissociation between knowing rules and using them to guide problem solving that we see in card sorting paradigms employed with younger children (Zelazo, 1996). Children in the very preterm group showed this behaviour more often. Examiner observations indicated that they would nod their heads when reminded of rules, but continue to disobey them. Such behaviour suggests an immaturity in the ability to coordinate complex task requirements or perhaps an inability to coordinate two rules in working memory at once.

As children proceed to the 3-move level of the task, requirements become more complex in that children must inhibit the tendency to place a disk on the most immediate goal-position peg (Fireman, 1996). Specifically, this move-level required children to remove a smaller disk and place it on a ‘holding peg’ while moving the larger disk to the goal post, a strategy which temporarily moves one away from a state that is visually similar to the goal (Baughman & Cooper, 2007). Observations and comments from children suggested that this required a cognitive leap in that they had to generate a prospective plan about how to overcome the obstacle of the smaller disk. Several children commented, “What do I do with this little one?” or, “If I put the big one on the little one, I’ll break the rules.” It is thus unsurprising that several children were unable to complete this level. Interestingly, once children had passed this level, few failed the 5-move level of the task, which required a similar appreciation of the available reserve peg. Instead, most of these children failed at the 7-move level, which is often employed in studies with adults. These adult studies have shown that one commonly-used strategy for this task is a goal-recursion strategy, which involves solving smaller sub-goals within the larger goal (Simon, 1975). Thus, this level demands a new level of complexity and forward thinking that few children were able to master. Performance of both groups of children thereby suggests a gradual increase in the ability to employ rules, overcome obstacles and develop complex rule-based strategies for the performance of the Tower of Hanoi task, with group differences possibly suggesting an immaturity of these developmental processes amongst children born very preterm.

More detailed analysis of children's performance on the Tower of Hanoi task revealed differences in the reasons for task failure. There were strict criteria for passing a move level and moving to the next move level of this task. Children had to complete at least one of the two trials in the fewest number of moves possible without breaking rules. Despite gentle reminders, most children failed a given move level because they broke task rules on both of the trials administered. However, children in the full term group were more likely to fail for the other reason - namely, completion of the task within a greater number of moves than were necessary. Thus, it appears that children in the very preterm group were less likely to attempt to solve the task without breaking rules, suggesting that these children had more difficulty inhibiting their immediate response tendencies.

Unfortunately, the strict criteria employed for discontinuation of the Tower of Hanoi task meant that if children failed the minimum move criterion twice, the task was ceased and the child was considered to have failed that move level. While this enabled a more efficient use of time over a long assessment session, it also prohibited the exploration of whether groups would show differences in their ability to self-correct their strategies. Mellier and Fessard (1998) found that children born very preterm often self-corrected their incorrect approaches to the Tower of Hanoi task at 12 years of age, eventually reaching the correct solution through trial and error. A similar approach in the current study would have allowed for the consideration of self-monitoring across the groups. Such information would be useful for educational purposes, in that it would help to determine whether children of this age would be likely to achieve the correct solution, given time and assistance. Given reported differences on this task, more in-depth studies of the executive strategies that children born very preterm employ when tackling this task would be useful.

Again, findings from the Tower of Hanoi are in keeping with previously documented differences in planning ability amongst children born very preterm (Anderson et al., 2004; Harvey et al., 1999; Luciana, 1998; Taylor et al., 2004). They are in close agreement with the findings of Taylor et al. (2004), who showed that adolescents born ELBW (<750g) spent shorter periods of initial time planning their responses on this task, suggesting a more impulsive approach. Given the much younger age of children in the current study, results suggest that these planning difficulties can be identified early. In that the Tower of Hanoi task requires a number of executive resources that are common to many problem-solving activities, findings are likely to reflect real-world differences in the ability of children born very preterm to initiate, plan, monitor, inhibit and reassess their own performance. Such skills are integral to everyday life and are likely to have significant bearing on children’s achievement at school.

Visual Search. The third measure of executive function included in this battery of tests was a visual search measure, which required children to search an array of visual stimuli and identify specific target items. Findings from this task showed that children in the very preterm group were more likely to make incorrect responses by selecting items that were not targets or by failing to identify target items. Therefore, they were less accurate overall. This suggests a difficulty in selectively focussing on target stimuli and in inhibiting a response to stimuli that are inappropriate.

Another interesting finding from this task is that children in the very preterm group were less likely to persist with searching. As opposed to taking longer to select items, as might be expected from the results of existing studies using this measure (Bohm et al., 2002; Bohm et al., 2004) and from the fact that some of these children had motor impairments, children in the very preterm group spent a significantly shorter amount of time completing this task. Unlike other tasks, children were able to elect how much time they spent searching the array of stimuli. A well-established body of evidence now indicates that children are active and intentional in the attentional strategies they use when completing visual search tasks (Wood, 1998). Younger children have been found to be less likely to make an exhaustive search, but instead base their decisions on one aspect of the visual stimulus array. In contrast, older children scan pictures in a more strategic and systematic way before making decisions. They appear to have an implicit plan on which they base their attentional search (Ruff & Rothbart, 1996). The failure of children in the very preterm group to persist with searching, coupled with their lower performance accuracy, may indicate reduced use of these executive monitoring and planning behaviours. Initiation, sustained attention and self-monitoring are essential features of executive function (Gioia et al., 2001; Miller, 2005; Stuss & Alexander, 2000; Zelazo & Muller, 2002). In many ways, then, the discrepancy in group times offers additional information regarding the executive difficulties of these children and will be an interesting factor to consider in future research. It is likely that this lack of persistence and error-checking will have significant bearing on children's everyday problem-solving and achievement.

In general, results for the Visual Search measure correspond somewhat with those of other researchers, who have demonstrated performance discrepancies on similar tasks (Bohm et al., 2002; Pasman et al., 1998; Vicari et al., 2004). Similar to findings from the present study, Marlow et al. (2007) found that children born extremely preterm (<26 weeks GA) engaged in more off-task behaviour during the completion of the same visual search task, indicating that extremely preterm children showed less sustained and focussed attention during task completion. Although the sampling frames for the Marlow et al. (2007) study and the current study are different, findings do converge in suggesting that sustained and focussed aspects of attention regulation are particularly difficult for children born very preterm and may underlie difficulties in the completion of visual search tasks.

Nonetheless, one confounding issue to consider in the interpretation of findings for this task is that poor performance may relate to underlying visual processing difficulties, as opposed to executive function. A recent study (Jakobson, Frisk, & Downie, 2006) showed that children born very preterm (<32 weeks GA , age 5- 6 years) had difficulty in recognising and responding to stimuli that were motion-defined (i.e. determining the direction of a stimulus when it is amongst an array of moving dots), as well as difficulty on several other tests of visual-motor processing, including difficulties with the same visual search task employed in the current study. Given the type of visual skills that were shown to be impaired in these children, these researchers argue for a disruption of the dorsal stream, the circuit in the brain responsible for determining where objects are located in space. The study also showed that children with mild forms of ROP and/or mild periventricular brain injury (determined by cranial ultrasound) were impaired on the visual processing tasks, while other children born very preterm showed performances similar to a full term comparison group. Such findings are of importance, and suggest that differences in the accuracy of performance on visual attention tasks may be related to difficulties in processing visuo-spatial information. In future, studies may benefit from pairing visual with auditory attention tasks to help determine which specific areas of attention may be more vulnerable.

Inhibitory Control/Set-shifting. Further areas of executive function assessed in this study included inhibitory control and cognitive flexibility/set shifting. On the Detour Reaching Box task, a task that required children to inhibit one strategic response and replace it with another, some group differences were also apparent. When considered as a whole, it was clear that children in the very preterm group were more likely to make errors on this task. However, the task involved a number of different phases, which yielded different findings for group comparisons. The first phase, which required children simply to reach into the box and obtain the ball, was easily passed at age 6 by all children. During the second phase, which required children to use a turning handle to obtain the ball, most children made few errors and were able to graduate to the third phase. Despite this high pass rate of children born very preterm, they were almost twice as likely to make an error on this phase by reaching directly into the box, as opposed to using the necessary strategy. Similarly, during the third phase, which required a switch to a new strategy, children in the very preterm group were 3 times more likely to reach directly into the box and were almost 7 times more likely to return to the former method of obtaining the ball. Persistent errors of inhibitory control and switching such as this resulted in 13% of children in the very preterm group being unable to graduate to the fourth, final phase of the task. These findings are similar to those of Hughes and Russel (1993), who found that this ‘switching’ phase of the Detour Reaching Box task was most difficult for children, with only 45% of children aged 3 to 4 years passing within three trials. The researchers suggested that this part of the task assessed the ability to disengage one’s attention from an object, with difficulties reflecting rigidity in attention. As Davidson, Amso, Anderson, and Diamond (2006, p. 2039) contend, it is often more difficult to suddenly switch cognitive strategies than it is to continue with a repeated response. This would suggest that children born very preterm might have more difficulty in flexibly disengaging a repeated response tendency.

However, as previous studies that have used this task have generally included younger samples (Hughes et al., 1998; Hughes & Russell, 1993), a third, more complex phase, which involved flexibly alternating one rule-based strategy with another, was incorporated in the Detour Reaching Box protocol for the current study. Surprisingly, during the completion of this final phase of this task, children in the very preterm group did not perform more poorly than their full term peers. This may be for several reasons. First, this task may have been trivially easy for most children by age 6 years. In general, children made few errors on the initial trials of the task, with rates of completion much higher at age 6 than was reported at 4 years of age (Edgin et al., 2008). Thus, those who did have difficulty may have dropped out by failing earlier trials, leaving only children who had no difficulty. This explanation seems implausible, given that approximately 60% of children in the full term group made at least one shifting error during this final phase, suggesting that they had some difficulty.

Second, the difficulties children born very preterm showed on the former phases of the task may have been related to learning or retaining new information. In accordance with a connectionist approach to higher level cognition (Johnson, 1998), children born very preterm may have taken longer to build up a memory trace for the task. However, once a memory trace had been established, their performance may have been no different from their peers. This may prove a useful area for future investigation in that it suggests that, with sufficient practice, children born very preterm may be better able to retrieve and utilise information more efficiently.

A third explanation for these findings may be that the relatively swift alternation between different strategies that was required for the final phase of the task meant that insufficient time was afforded in which to build up a prepotent response. To elaborate, the final phase of the Detour Reaching Box task required rapid alternations between response strategies. This type of task may actually require less inhibitory control in that there is less proactive interference from a competing response tendency. By contrast, the first and second phases of the task, where children had been preliminarily conditioned to respond in a particular way, and then were required to override this tendency, may have been more difficult.

As such, results from the Detour Reaching Box can neither support nor disconfirm findings of spared set-shifting ability in some studies of children born very preterm (Espy et al., 2002; Landry et al., 2002; Taylor et al., 2004). Future studies may need to compare the effects of greater working memory requirements, vary the number of trials before set shifting is required, as well as examine developmental changes in order to more effectively resolve this issue. Future studies may also benefit from stratifying samples so that the impact of a more severe perinatal course may be examined.

Sustained Attention. The final laboratory-based measure employed in this study was a version of the Continuous Performance Task designed for use with young children. This measure was chosen to assess the ability to maintain vigilance and focus and also to inhibit responses to inappropriate targets. Given that children born very preterm are approximately 3 times more likely to be diagnosed with ADHD (Bhutta et al., 2002) and such measures have successfully distinguished children with clinical diagnoses of ADHD in the past (Barkley, 1997), this measure was thought to be appropriate for assessing such dimensions in this population. In particular, children with ADHD have been found to have longer response times and to make more errors of omission and commission on this task, suggesting a difficulty in inhibiting motoric responses (Epstein et al., 2003).

Surprisingly, findings showed that children in the *full term* group made more errors of commission on this task. In contrast, children in the very preterm group were more likely to make errors of omission, failing to respond to stimuli when appropriate. They also took longer to respond to stimuli on this measure. A closer examination of the results showed that children born full term tended to make more errors of commission during blocks of trials in which children born very preterm made more errors of omission. This suggests that the significant elevation in commission errors in the full term group may reflect the fact that children born very preterm were tending to pay less attention to the task or were unable to process and react to stimuli quickly enough.

Differences may be due to the developmental level of the sample. Go/no-go tasks such as this have seldom been used with younger samples of children. In one study of children aged 5-6 years, similar findings were obtained in that children with ADHD were more likely to make errors of omission, as opposed to errors of commission (Kalff et al., 2005). It may be that children with attentional weaknesses are unable even to sit and complete the task effectively at this young age, indicating that our interpretation of findings needs to account for developmental timing. Such differences suggest that young children born very preterm have impairments in the sustained, focussed aspects of attentional control.

Similar findings have been reported in two other studies of executive function in older children born very preterm. For example, in a study of 11-yr old children who were born <2000g, Elgen et al. (2004) found that the rate of omission errors on a Continuous Performance Test was double that of a full term control group, with no group differences in terms of commission errors. As in the current study, the standard deviation for this measure was also higher amongst children born very preterm, suggesting increased variability in their task performance. Similarly, Nosarti et al. (2007) found that young adults who had been born very preterm were no more likely than a group of full term born adults to make errors of commission or omission across different computerised measures of attention. Rather, these adults tended to show an erratic pattern of latency to respond, occasionally showing very long response speeds relative to their mean response times. The researchers suggest that this may reflect a greater number of attentional lapses, although it may also suggest slowed processing speed. Therefore, both studies are generally consistent with the current study in suggesting that difficulties in sustained, focussed attention may contribute to the poorer performances of children born very preterm on vigilance tasks.

Interestingly, behavioural studies of children born very preterm have often suggested a lack of confounding oppositional and conduct disorder when these children are diagnosed with ADHD, which is dissimilar to the high rates of comorbidity for these diagnoses in the general population (Johnson, 2007). Some behavioural researchers have also suggested that children born very preterm may be susceptible to a more ‘pure’ form of attentional disruption, with less likelihood of hyperactivity or impulsive behaviour

(Elgen, Sommerfelt, & Markestad, 2002; Indredavik, Vik, Heyerdahl, Kulseng, & Brubakk, 2205). Therefore, the current performance-based findings are also coherent with behavioural reports.

There is the possibility that the slow motor responses of children born very preterm caused them to miss targets on the K-CPT. Insofar as it was possible, an attempt was made to statistically control for motor impairment by reconducting statistical analyses excluding children with moderate to severe motor impairments. However, more subtle motor impairments are also more likely to be associated with very preterm birth and recent research with children who have attentional problems has suggested that these difficulties often co-occur with attentional difficulties (Jeyaseelan, O'Callaghan, Neulinger, Shum, & Burns, 2006; Piek et al., 2004; Sargeant, Piek, & Oosterlaan, 2006; Wassenberg et al., 2005). Certainly, common neural substrates have been identified as contributing to both motor and attentional control (Casey et al., 1997), increasing the likelihood that children with neurological abnormalities will show difficulties in both of these areas of functioning.

One factor that must be taken into account in the consideration of findings for this measure is that children may have had different experiences with computers. It is highly likely that many of the study children would have access to computers in their homes. Differences in individual experiences with computers may have induced practice or novelty effects. In comparison to the games that some children may have had experience with at home, this vigilance task may have been tedious and uninteresting. Therefore, they may not have invested as much effort. Others may have enjoyed the novelty of access to a computer and therefore invested more effort. This may well have affected individual performance.

Executive Behaviour. This study also incorporated behavioural measures of executive function, including parent and teacher questionnaire measures, as well as examiner consensus ratings of children's behaviour during their developmental assessment. Such measures strengthen the validity of the study in that they provide independent sources of information, as well as information about whether the performance differences identified by laboratory measures are evident in the context of everyday experience.

Across all of these behavioural measures, children in the very preterm group were found to show greater levels of executive impairment. In particular, parents rated children born very preterm as having more difficulties across multiple areas of executive function, with effect sizes tending to be higher for metacognitive measures of planning, initiation, working memory and set shifting. This was also the case for teacher ratings based on the same measure. Teachers were more likely to nominate working memory, planning, initiation and shifting as being areas of difficulty for children born very preterm, with emotional regulation being rated at similar mean levels to full term children.

This tendency for parents and teachers to nominate children born very preterm as having greater difficulties on the metacognitive measures of the BRIEF was also shown in a study of children born ELBW (<28 weeks GA) at 8 years of age (Anderson et al., 2004). While significant differences were found in parental ratings of shifting, working memory, planning and monitoring, parents did not rate children as having more emotional difficulties or difficulties with inhibitory control in everyday life. It may be that these findings reflect a relative sparing of the emotion regulation aspects of executive function, perhaps mediated more by orbitofrontal-limbic circuits within the brain. However, it is also likely that these differences are reflective of an increased emphasis on 'cool,' cognitive aspects of executive function that may be more noticeable and of increased concern for teachers and parents at this school-going age.

Although they were not standardised, the behavioural consensus ratings used in this study were a useful adjunct to other measures. Duncan (1986) has argued that patients with different neurological lesions may fail the same task for different reasons. In the case of patients with frontal lesions, these reasons may be different from those with lesions to other areas. Therefore, similar performance may come about even when there are different underlying processes. An analysis of the behaviours during task performance is therefore integral to interpretation of task performance. The behavioural ratings in this study supported the idea that children born very preterm did not show the same levels of strategising, were less inhibited and showed less self-monitoring than their peers. This adds weight to evidence from the task measures and strengthens the argument for global impairments in executive function and self-regulation amongst children born very preterm.

Taken together, findings for the executive function tasks support the first hypothesis of this thesis. Examination of the performance of children born very preterm on a variety of measures of executive function suggested that impairments were diffuse and pervasive, with between group discrepancies evident across all measures administered. An exception was the inhibitory control element of the K-CPT. Descriptive analyses of the performance of each group on measures of executive function also showed that controlling for the potential impact of more severe neurodevelopmental difficulties did not alter the general pattern of between group differences in performance. Children in the preterm group without these severe impairments performed more poorly on measures of executive function than those in the full term group. Statistical control for SES differences between groups also did not account for the relationship between very preterm birth and poor executive function performance. These findings suggest that discrepancies in the executive function of children born very preterm and full term are not the result of more severe impairments in a minority of these children and cannot be explained by the effects of SES.

Specific comparisons can be made with several existing studies. For example, a recent study by Marlow et al. (2007) showed that children who had been born extremely preterm (<26 weeks GA) showed difficulties in all executive domains tested at age 6 years. Like the current study, measures included a tower task and a visual search task. The researchers also administered tests of motor inhibition, including a ‘knock and tap’ task and a task involving resistance to distraction. Small differences in scores were noted across all of these measures when children were compared to their peers, with differences being approximately half a standard deviation in overall magnitude.

Findings from this study are also similar to those described by Talyor et al. (2004), although their study was conducted with a much older sample (14-21 yrs). These researchers found large differences in performance between a group of adolescents born ELBW (<750g) and a full-term control group on a number of measures of executive function, with children born VLBW (750 -1500g) performing at a more intermediate level. Based on measures of standard error, adolescents in the VLBW group were more likely to have difficulties in spatial span, while those in the ELBW group were more likely to have difficulties across measures of block design, visuo-motor skills and executive function, but not more likely to have difficulties in vocabulary or language pragmatics. Similar to findings from the present study, when adolescents with IQ scores less than 70 or neurosensory impairments were excluded from analyses, mean differences in verbal memory and language-based measures did not persist. Such findings are in keeping with those from the present study in suggesting that very preterm birth places one at risk for both global and more subtle impairments, with more subtle impairments appearing to be more prevalent in areas that require visuo-motor integration and fluid problem-solving. Insofar as specific difficulties may be present over and above a general, more diffuse pattern of cognitive difficulties, it seems that these skills are more promising targets for future research and intervention efforts.

11.1.3 Relationships Among Measures of Executive Function

Following the identification of consistent, pervasive difficulties in executive function amongst children born very preterm, the relationships in performance across laboratory tasks related to this construct were explored. This analysis was performed in a similar way to studies with non-clinical samples and supported the “unity”, as well as “diversity” of executive function as a construct (Miyake et al., 2000, p. 49). Correlations and principal components analysis supported a single latent construct assessed by these measures, but this latent construct was weak and did not explain the majority of variance in task performance. There was also indication of a division of tasks into those that were selected to assess working memory and those selected to assess attentional control and cognitive flexibility. In contrast, the Tower of Hanoi task and Visual Search tasks appeared to be associated with both of these broader divisions. These findings tend to be consistent with other studies in supporting separate dimensions of working memory/updating and set-shifting, but not inhibitory control (Huizinga et al., 2006; van der Sluis et al., 2007).

The finding that the Tower of Hanoi seemed to show relatively equivalent relationships with all other measures is consistent with the idea that effective completion of this task requires a complex utilisation of multiple executive skills. In a study of executive function in adults, Miyake et al. (2000) found that the Tower of Hanoi task was related to tasks assessing inhibitory control, but also argued that all executive function tasks involved the maintenance of goal-related information in working memory. In samples of children, the Tower of Hanoi has tended to load on a separate factor, often labelled ‘planning’ (Klenberg et al., 2001; Levin et al., 1991; Welsh et al., 1991). Computational models of the tower tasks have also shown that both strategy and inhibitory control are required for effective performance on the Tower of Hanoi (Baughman & Cooper, 2007). The factor analytic findings of the present study suggest that the performance of young children on the Tower of Hanoi task is influenced by both working memory and executive attention, highlighting the complexity of task demands.

However, overlaps between findings from these studies and the current study may be restricted in that former factor analytic studies have examined executive function in normative samples. In the current study, there were some differences in the factor analytic findings across the two study groups. Specifically, correlations between working memory tasks were stronger in the full term group than in the very preterm group, perhaps indicating a greater divergence of verbal and spatial working memory in the very preterm group. Within the very preterm group, performance on the Visual Search task was more robustly correlated with performance on the working memory measures. In contrast, in the full term group, this task was more closely related to the Detour Reaching Box and CPT measures. This is a curious finding. The Visual Search task was selected to assess selective attention, which suggests that it should, theoretically, have correlated with the measures of sustained attention and flexibility. However, within the very preterm group, it is possible that children had more difficulty remembering the items they were searching for, which would have changed the nature of this task for these children. In particular, the second visual array of stimuli was very complex visual array, with differences in stimuli (black and white drawings of faces) being quite difficult to detect. It is conceivable that this array would have placed increased demands on the ability to remember the target stimuli and in turn, may have placed higher executive working memory demands on children in the very preterm sample. Such a conclusion is also supported by an fMRI study showing that older children born very preterm recruited a wider, more diffuse array of neural circuits when engaged in a go/no-go task (Nosarti et al., 2006), suggesting that children born very preterm may need to draw on more cognitive resources when engaged in complex executive processing. Group differences in these factor analytic findings may therefore reflect differences in the underlying executive processes employed by children born very preterm in order to complete these complex tasks.

However, it should be noted that factor analysis is susceptible to misspecification and relies on interpretation of results. Additionally, it is important to remember that executive function tasks, in their complexity, no doubt capture a number of other skills (Frith et al., 2004). In light of these issues, there are alternative explanations for the 2-factor solution suggested by the factor analyses completed. First, given that correlations between executive performance measures within the full term group were slightly lower, it is possible that correlations between measures really reflected global cognitive impairment (i.e. the most severely impaired children did not perform well across any measures, thereby making measures appear correlated). Second, it is possible that the division of tasks reflected a greater reliance on motor skills or quick and fluent responses for performance on the Detour Reaching Box and CPT. Finally, it must also be noted that the environmental circumstances changed somewhat with the administration of the computer-based K-CPT task, because the examiner left the room. Thus, while children may have been scaffolded somewhat by the supportive presence of the examiner for other tasks, the absence of this support and encouragement may have affected children's performance, causing some children to perform differently from how they would have performed when the examiner was in the room. The decision to divide task measures into those involving working memory and planning abilities and those involving executive attention skills may therefore be seen as interpretive, with alternative suggestions clearly viable.

Notwithstanding these limitations, results suggested that dividing measures into two overall factors would enable more reliable conclusions. Whilst it would also have been feasible to combine all tasks as one measure, a 2-factor solution was able to capture more task variance. Unfortunately, this meant that the second factor, created from two tasks, was less robust and reliable than the first. It was important, however, to include this composite because it reflected performance on the sustained attention component of the K-CPT, a measure that showed moderate effect sizes for between-group differences. In further support for a two-factor solution, subsequent analyses confirmed that the two factors were related to different antecedent medical and socio-familial experiences within the very preterm group.

11.1.4 Clinical, Neurological and Socio-Familial Predictors of Later Executive Function in Children born Very Preterm

An examination of the clinical, neurological and socio-familial factors associated with the later 1) working memory/planning and 2) executive attention competence in children born very preterm suggested that there were both commonalities and differences in the antecedent factors associated with each of these overall domains. On both the working memory and the executive attention factor, males performed less well than females. This association with gender remained robust, with no attenuation after consideration of other clinical or medical factors. These findings are in keeping with evidence showing that males tend to be more vulnerable to perinatal brain injury, cerebral palsy and congenital abnormalities than females (Kraemer, 2000; Raz et al., 1994). There is also evidence to suggest that male children born very preterm are more vulnerable to cognitive and behavioural impairments than females, even when subject to similar medical and neurological experiences (Lauterbach, Raz, & Sander, 2001; Raz et al., 1995). Findings from other studies assessing executive function in relation to gender have also shown that preterm boys achieve lower scores on laboratory and checklist measures of attention (Elgen et al., 2004; Marlow et al., 2007; McGrath et al., 2005).

While there is no consensus regarding why males appear to be more vulnerable, there is some suggestion that neurological and pulmonary maturation in males is slower. This may place them at increased susceptibility to the medical and neurological factors associated with prematurity, even when they may be the same chronological age as their female counterparts (Lauterbach et al., 2001; Raz et al., 1995). Furthermore, differences in recovery from hypoxia may be due to higher levels of catecholamines, an important chemical defence mechanism, in the blood of female infants born very preterm

(Ingemarsson, 2003). While this study could not ascertain a reason as to why males appeared more vulnerable than females, it does agree with former studies in suggesting that male gender may be an independent risk factor for later executive impairment and is probably related to differences in the maturity or potential for recovery in each gender, as opposed to differences in exposure to medical interventions.

Other perinatal risk factors associated with poorer working memory/planning performance within the very preterm group included evidence of maternal infection and the extent of white matter abnormality evident on term MRI scans. The demonstration of an association between these factors is exciting because such findings support current theories relating to the mechanisms of neurological injury in children born very preterm. Specifically, two pathways for the development of white matter abnormality in the very preterm infant have been implicated. These include 1) the ischemic pathway, whereby reduced oxygen availability leads to necrosis of cells and 2) the inflammatory pathway, whereby infection to the foetal membranes evokes an inflammatory response in the foetus, which in turn results in the release of cytokines, causing damage to immature oligodendroglia (Arpino et al., 2005; Back, 2006; Damman, Kuban, & Leviton, 2002). In support of this, studies using animal models have shown that the administration of e coli or endotoxin lipopolysaccharide during gestation leads to a diffuse pattern of white matter injury consistent with the pattern seen after very preterm birth (Rees & Inder, 2005). Similarly, there is support for a relationship between maternal infection and cerebral palsy in children born very preterm (Bax, Tydeman, & Flodmark, 2006). Therefore, there is strong theoretical and some research support for a relationship between maternal infection and white matter abnormality.

In the current study, the relationship between indicators of maternal infection and working memory/planning difficulties was slightly attenuated when white matter abnormality was accounted for, supporting a mediational pathway. However, the relationship was not completely attenuated. These findings may support the hypothesis (Dammann et al., 2003) that infection also has an effect on synaptogenesis, dendrification and, importantly, on neural function, all of which would be unlikely to be apparent on qualitative, structural MRI measures.

Unfortunately, it is probable that the small group of infants whose mothers were feverish or who did show signs of maternal chorioamnionitis are under-representative of a larger group of infants who may have been subjected to unrecognised infection. Coupled with this, theorists have suggested that hypoxia-ischemia may still be implicated in that it may lead to inflammation and cytokine release (Arpino et al., 2005). In this case, overt signs of infection may not be apparent, despite an inflammatory response in the foetus.

Relationships between working memory/planning and white matter abnormalities suggest long-term effects of early non-cystic, diffuse white matter abnormalities on subsequent higher-level cognitive development. These results add to a growing body of evidence suggesting that early injury or alteration in developing white matter may have substantial impact on children’s later cognitive ability (Anderson, 2007). They also add to existing literature showing relationships between ultrasound measures of IVH and PVL and executive function (Frisk & Whyte, 1994; Ross, Boatright et al., 1996; Roth et al., 1993; Sherlock et al., 2005).

The long term effects of white matter abnormality demonstrated in this study may be the result of reductions in myelination due to damage to precursor cells. White matter injury may have long-term consequences for the integrated circuitry of the neural system. In terms of the early impact of white matter damage, diffusion tensor imaging studies have found that white matter injury corresponds with an alteration in the organisation of fibre tracts within the infant brain, suggesting that injury has a major impact on the organisation of axons within regions that are essential for information processing (Huppi et al., 2001; Miller et al., 2002). Increases in white matter, presumably reflecting myelination, are predominantly responsible for neural growth over middle childhood (Sowell, Trauner, Gamst, & Jernigan, 2002). As the most commonly recognised neurological consequence of very preterm birth is a diffuse form of injury or abnormality of white matter areas in subcortical regions (Perlman, 1998; Silveira & Procianoy, 2005; Volpe, 2001a), isolated damage to the prefrontal cortex is unlikely to underlie difficulties in the performance of executive function tasks. Instead, it is likely that the injury to white matter affects the connectivity and integration required for effective communication between neural systems, resulting in slower information processing and less efficient executive control.

In contrast to these clear associations between qualitative ratings of white matter development and later working memory/planning, qualitative ratings of the maturation of gyri and cortical volume at term did not correlate with later executive function performance. As mentioned in the introduction, studies of development in adolescents born very preterm have described associations between volumetric measures of grey matter volume and cognitive performance measures, although relationships are not consistent (Abernethy et al., 2004; Gimenez, Junque, Narberhaus, Botet et al., 2006;

Isaacs et al., 2000; Peterson et al., 2000; Stewart et al., 1999). Therefore, it was expected that similar correlations would emerge in the current study. However, the studies cited above have conducted MRI and neuropsychological assessments simultaneously. One explanation for the lack of correlation between measures of grey matter abnormality and executive function in the current study may be that early injury to white matter also affects the ongoing development of grey matter that may be more clearly evident at older gestational ages than at term.

To elaborate, it is likely that injury to key structures and ventricular dilation within the ventricular region where white matter injury often occurs will have consequences for later neural development (Volpe, 2003). Recent imaging studies support an association between white matter and grey matter abnormalities (Boardman et al., 2006; Counsell et al., 2007). Boardman et al. (2006) showed significant associations between levels of diffuse white matter abnormality in children born preterm and volumetric reductions in the thalami and the lentiform nuclei at term equivalent age. These areas are of central importance in the processing of information to and from higher cortical areas. A further study showed that white matter abnormalities on MRI scans within the first two weeks of birth were followed by reduced grey matter volume at term age (Inder et al., 1999). Thus, the lack of correlation between early measures of grey matter abnormality and later executive function in the present study may well mask a cascading effect of early white matter damage on subsequent neural development.

It is nevertheless important to consider that children's performance on the composite measure of sustained attention and inhibitory control/set-shifting did not show the same linear relationships with severity of cerebral white matter abnormality. Instead, there was a general indication that infants who had been least mature at birth performed less well on the measure of executive attention, with medical risk factors such as PDA, ROP and respiratory complications also related to poorer performance in this domain at age 6 years. One reason for this may be that the qualitative ratings from neurological scans are not sufficiently sensitive to detect functional neurological abnormalities. However, it is also possible that different mechanisms may account for the altered development of these executive processes.

Differences in the developmental factors that were associated with the two overall areas of executive function also call into question the idea that the deficits in executive function that we see amongst children born very preterm are mediated primarily by neurological abnormalities. While such theories are appealing, maternal stress during pregnancy, as well as infant autonomic immaturity, may offer alternative or additive mechanisms for the disruption of children's arousal and homeostasis (de Weerth & Buitelaar, 2005; Feldman & Eidelman, 2007; Talge, Neal, Glover, & Early Stress Translational Research and Prevention Science Network, 2007; Van den Bergh, Mulder, Mennes, & Glover, 2005). The attentional difficulties we see in children born very preterm may be related to regulatory difficulties, perhaps associated with early disruption of the hypothalamic-pituitary adrenal (HPA) axis through repeated exposure to pain or stress. In support of this, studies have shown correlations between higher levels of parenting stress, higher levels of intrusiveness, higher levels of basal cortisol and lower levels of focussed attention in infants born very preterm, suggesting complex interactions between these biological and social risk factors (Thanh Tu et al., 2007). There is also some suggestion that children born very preterm may show differentially higher levels of cortisol when their parents show high levels of depression (Blunt Bugental, Beaulieu, & Schwartz, 2008), suggesting a greater vulnerability to environmental stress factors in this group of children. These relationships require further replication, as other studies have shown down-regulation of the HPA axis in extremely preterm infants who have been exposed to greater levels of pain during the neonatal period (Grunau et al., 2005). Nonetheless, it is conceivable that the disruption of the HPA stress system is an important factor underlying executive function difficulties.

In summary, executive outcomes amongst children born very preterm were correlated with neurological integrity, and particularly with white matter pathology, at term age equivalent. However, this association appeared to be more robust for measures that relied on ‘cool’ cognitive planning and working memory aspects of executive function. For measures that were more related to sustained attention and behavioural inhibition, lower gestation at birth appeared to show a stronger relationship with later performance.

Despite the inclusion of various measures of social risk, there were no significant relationships between these measures and measures of executive function performance amongst children born very preterm once clinical factors were accounted for. Specifically, SES, single parenthood, young maternal age, self-reported maternal depression or anxiety and family stress did not correlate with either executive composite measure. While household poverty (income <$25000) at age 6 years was associated with performance on executive working memory and planning tasks, income did not emerge as a significant factor within the overall model of antecedent predictors. These findings are surprising, given that the social background factors chosen for study are well described as risk factors in developmental literature (Sameroff et al., 1993). However, they do correspond somewhat with recent findings of Taylor et al. (2006), who showed that although SES and family stress were related to executive function in children born ELBW (<1000g), they did not moderate outcomes when children were compared to their full term peers. These researchers suggest that the effects of medical risk may overwhelm any subtle associations between environmental factors and executive function.

One factor that did emerge as a predictor of children's working memory and planning performance was the degree of parental change or instability they had experienced across the period from birth to 6 years. Children who had experienced more stable, continuous parenting performed better on measures of working memory and planning than those who had experienced one or more changes in parent. Generally, parental changes were the result of marital separation or divorce and partner changes. For the most part, findings are in agreement with mainstream developmental research showing that parental separation is associated with poorer academic and behavioural outcomes in children (Amato, 2001; Hetherington, Bridges, & Insabella, 1998). Added to this, recent evidence suggests that environmental instability, including changes of residence, changes in parental figures or loss of parents, can have sustained negative effects on children's development (Adam, 2004). The experience of chaos within the family system is likely to challenge the coping resources of both parent and child, limiting their available resources for fostering a secure, regulated relationship that might allow the child to explore and learn. In the current study, maternal depression and anxiety, SES and financial status were also correlated with incidences of parental change, suggesting that family instability operates amidst a cluster of disadvantageous circumstances.

While few of the more distal socio-familial measures were significant in predicting children's performance on measures of executive function, measures of parenting behaviour, assessed at ages 2 and 4 years, were some of the strongest predictors of working memory/planning and executive attention scores at age 6 years. Specifically, maternal sensitivity and intrusiveness were associated with working memory/planning performance, while intrusiveness alone was associated with children's executive attention. Children whose mothers were sensitive and responsive to the cues of their children, setting up tasks so that children could easily select materials, encouraging children and asking leading questions that were contingent on the child's activities, were more likely to obtain higher working memory/planning scores at age 6 years. In contrast, children of mothers who had been over controlling and disruptive of children's fluent activity during early problem-solving interactions were likely to obtain lower scores on measures of planning/working memory and attention at age 6 years. Similarly, higher levels of mutual synchrony observed between parent and child during these observations were associated with higher working memory/planning performance.

These findings support a theoretical argument for the co-construction of self-regulated problem solving (Vygotsky, 1978). Consistent relationships between maternal levels of intrusiveness and children's executive function are in accordance with theories that emphasise the importance of scaffolding that is child-centred and that works in accordance with the developmental requirements of the child by building on or supporting the child's own focus of attention or interest (Bronson, 2000; Meadows, 1996; Warren & Brady, 2007). Intrusive strategies may encourage compliance in the child, but they are also likely to discourage self-regulation, motivation and initiative (Bronson, 2000; Meadows, 1996). Behaviours that are intrusive are also likely to discourage joint attention, an important precursor for children's development of sustained attention and regulation, because they are overstimulating and aversive for the child (Landry, Smith, & Swank, 2006). In contrast, it is likely that sensitive, responsive parenting rewards children for their enthusiasm and initiative, fostering the development of independent planning and assisting children to learn that environmental effects are contingent on their actions.

Robust relationships between early parenting behaviours and later executive function are consistent with the small body of literature documenting such linkages in groups of children born very preterm (Assel et al., 2003; Landry et al., 2002). These studies have suggested that early parenting sensitivity is related to later executive function and mathematical performance within children born LBW. However, the former studies examined the effects of parenting on healthier and heavier children of low SES. Therefore, the current study extends upon past findings, helping to clarify the importance of parenting for executive function development in a more representative sample of children born very preterm.

However, in the context of very preterm birth, it is very important to consider the mutual, transactional dynamic between parent and child. Several studies of children born very preterm have shown that they display increased levels of both hypo and hyper-arousal (Eckerman, Hsu, Molitor, Leung, & Goldstein, 1999; Feldman, 2007). For example, children born very preterm have been found to display more negative affect in interactions, especially when over-stimulated (Eckerman et al., 1999). They have also been found to be more difficult to calm and soothe. Thus, they can be placid and unresponsive, while at the same time becoming easily dysregulated and disorganised in their responses (Hughes, Sults, McGrath, & Medoff-Cooper, 2002). As a result, signals from these children are probably more difficult to read. Coupled with this higher reactivity and emotional lability in children, parents of children born very preterm have been found to have higher levels of anxiety, stress and depression (Davis et al., 2003; Shandor-Miles et al., 2007; Singer et al., 1999), which is also related to decreased synchrony and responsiveness between parents and children (Feldman, 2007).

Difficulties in the temperamental demeanour of infants, coupled with a vulnerable psychological state in the parent, may create a mismatch in signals between parties. When children show more passive behaviour and a lack of attention or persistence, parents often respond by exerting more control and interactions become asynchronous (Feldman, 2007; Muller-Nix et al., 2004). Indeed, mothers of children born very preterm report concern over the provision of stimulation in order to try to compensate for vulnerability in their children (Shandor-Miles & Holditch-Davis, 1995). Such over-stimulation may lead to disorganisation in the child (Salonen et al., 2007). This may be even more relevant for children who are biologically predisposed to higher levels of reactivity. For instance, Landry, Garner, and Swank (1996) showed that children who were born LBW (<1600g) with high levels of medical risk (BPD or IVH) were more likely to decrease the complexity of their play when mothers redirected their attention. This suggests that the disruption of attention was more difficult to overcome for these infants than for infants exposed to lower levels of biological risk. Thus, even though parents are attempting to be responsive and warm, their behaviour may be inappropriate in the context of the child's needs. As a result, children are likely to respond by becoming increasingly dysregulated or unresponsive. These disrupted patterns of interaction are likely to act in a reciprocal manner, with mothers becoming progressively discouraged and interactions becoming more rigid, detached and stressful.

Similar patterns of interaction are found between parents and children with other forms of developmental compromise. For example, parents of children who are hyperactive and non-compliant are more likely to show intrusive and controlling behaviours. They respond less to positive behaviours in their children and attend more to non-compliant behaviours (Campbell, 1995). Studies of children with Down's Syndrome show that they are less likely to provide cues to their parents and are less likely to be appropriately scaffolded (Meadows, 1996). For instance, a recent study showed that children with Down's Syndrome were less engaged with and attentive to their parents from very early in life (8 weeks). In contrast, parents of these children did not differ from a control group in their levels of sensitivity towards their children. By 20 weeks, parents of children with Down's Syndrome had become more intrusive and remote, suggesting that their change in parenting style was a response to the characteristics of their children (Slomins & McConachie, 2006). Thus, it seems that the associations shown between parental intrusiveness and attentional regulation in children may emerge due to the transactional influences of parent and child characteristics. The salient issue is not who is 'responsible' for the lack of synchrony, but that children who are most in need of effective scaffolding are actually less likely to receive it (Meadows, 1996).

Collectively, the analysis of relationships between measures of antecedent factors and executive function at school entry showed that the second set of hypotheses for this thesis were partially supported, with some measures of early medical experiences, neurological abnormality and social experience showing small to moderate correlations with later executive function performance. Findings are illustrative of the complex, multidirectional processes that shape children's developmental trajectories, as well as the importance of a life-course perspective.

11.1.5 Associations between Executive Function and Academic Achievement at Age 6 Years

The final section of this study examined relationships between measures of executive function and measures of academic achievement amongst children born very preterm and children born full term. The study hypothesis was that group differences in executive function were likely to covary with differences in children's academic achievement. This hypothesis was based on research highlighting the importance of developing executive function for children's transition to schooling and their academic competence (Blair, 2002; Blair & Razza, 2007; Bull & Scerif, 2001; D'Amico & Guarnela, 2005; Gathercole et al., 2005; van der Sluis et al., 2007; van der Sluis et al., 2004). In support of this hypothesis, findings revealed strong associations between executive function measures and clinical and teacher-report measures of children's academic achievement.

The relationship between executive function and the Woodcock-Johnson measure of mathematics was particularly strong. There are several explanations for the substantial degree of overlap between early executive function and mathematics achievement. Interestingly, the parietal, prefrontal and cingulate regions of the brain, which have traditionally been associated with executive function, have also been found to be activated during arithmetic performance (Dahaene, Molko, Cohen, & Wilson, 2004). This suggests that performing mathematics engages executive functions. Indeed, mathematics requires self-regulation in order to prevent oneself from approaching a problem impulsively. Children can often approach mathematics with a high degree of impulsivity, failing to stop and think about their approach to a problem or to appreciate the constraints of the problem at hand (Wood, 1998). This was evident in the approach of a number of children in the current study when completing the simple addition and subtraction problems presented to them. An examination of their answer sheets and behaviour during testing showed that children often gained correct answers on the addition problems and continued to add numbers when presented with subtraction problems, failing to appreciate or notice the difference in mathematical symbols. Many other children, particularly in the very preterm group, wrote the same incorrect answer for all mathematical problems. In this case, children made a perseverative response as opposed to stopping and thinking their answer through. Perhaps this supports the notion that inhibitory control is the precursor for effective executive control (Barkley, 1997).

Children who have difficulties in mathematics have been shown to make more errors in computation, to use immature strategies and to take longer to reach solutions (Geary, 1993; van der Sluis et al., 2004). This suggests difficulties in the retrieval of information from long-term memory as well as difficulties in working memory, processing speed and strategising. Present study findings agree with previous studies in highlighting working memory as important for mathematics. Particular difficulties in spatial as opposed to verbal working memory suggest that children born very preterm have difficulty holding and manipulating information in the visuo-spatial sketchpad. This is likely to be problematic in the area of mathematics, where information has to be integrated, rules applied according to set mathematical procedures and information sequentially processed in accordance with a goal. The amount of information able to be active in working memory at once will be important to prevent memory ‘decay’ before a problem is solved (Geary, 1993). This was particularly evident in the performance of one child in the very preterm group. She counted fingers on her second hand and then forgot the number she had already counted on the former hand. Thus, even with the concrete assistance provided by her counting on her fingers, limitations in her ability to maintain several pieces of information in working memory had a visible impact on the speed and efficiency of her performance.

Difficulties in working memory may also affect long-term retention and learning of mathematical knowledge in that children with these difficulties will have fewer opportunities to filter correct answers to long-term memory (Geary, 1993; Sweller, van Merrienboer, & Paas, 1998). There is evidence to suggest that working memory is important for the understanding of mathematical concepts, acquisition of information and for counting and strategy use during the early school years. Specifically, the counting spans of younger children (1st grade) have been found to be associated with less use of finger counting or verbal counting and less counting errors, but this tapers off as children grow older and knowledge becomes part of long term memory (Geary et al., 2004). With repeated practice at computation, children who obtain correct solutions are likely to build up a more effective memory trace for the information. Thus, they are likely to achieve a degree of automaticity faster than those who repeatedly reach incorrect answers. This synergy between two memory systems potentially explains the strong relationship between children’s working memory/planning skills and their performance on problems that more competent mathematicians would be able to complete by rote.

Findings from this study overlap with those of other researchers (Bull & Scerif, 2001; D'Amico & Guarnela, 2005; Espy et al., 2004; van der Sluis et al., 2007; van der Sluis et al., 2004), who have also shown relationships between measures of executive function and mathematics achievement. For example, Bull and Scerif (2001) showed that individual variations in mathematics achievement on a standardised test were associated with executive measures of working memory, perseveration and inhibition. Similar to the current study, performance on executive measures contributed a small amount (about 3%) of unique variance over and above IQ and reading test scores.

Added to these associations with mathematics, there were also clear linear associations between measures of executive function and reading achievement across both groups of study children. However, group differences in reading were restricted to teacher ratings of reading achievement and did not emerge for standardised testing. These findings may indicate a developmental dissociation between different forms of working memory that may have implications for individual differences in learning. Specifically, results from this study, as well as the review of former studies presented in the introduction, suggest that children born very preterm appear to have greater difficulty in the visuo-spatial aspects of working memory. Although there was some indication of difficulty in the area of verbal working memory, the effect size for this difference was smaller and tended to be more specific to children with more severe cognitive impairment. There is some evidence also that children with reading difficulties may have difficulties with phonological loop processes and phonological working memory, with a relative sparing of more visual-spatial domains (Jeffries & Everatt, 2004; Pennington, 1991; Siegel & Ryan, 1989). By extrapolation, it may be that children born very preterm have a relative sparing of phonological memory processes, which in turn may allow for better performance in reading. Other researchers have also demonstrated patterns of impairment in children born very preterm whereby verbal skills appear to be relatively spared and performance-based or fluid skills differentially affected (Fazzi et al., 1997; Roth et al., 1993). It is possible that this pattern is part of a broader spectrum of neurological difficulties that affect visuo-spatial integration, attention, motor control and mathematics (Goyen et al., 1998).

In speculating about the mechanisms behind such a profile of impairment, we can turn to literature on children who demonstrate difficulties in mathematics. Some children struggle with arithmetic largely because of literacy (Rourke & Conway, 1997). Thus, mathematics difficulties often occur co-morbidly with difficulties in reading. Other children have difficulty with complex spatial reasoning, integration of concepts and executive function. These children appear to have more difficulty in understanding and conceptualising mathematics (Pennington, 1991). Neuropsychological evidence from adults and children has shown consistent relationships between these difficulties and structural abnormalities in the right hemisphere of the brain (Byrnes & Fox, 1998; Pennington, 1991). Interestingly, the right hemisphere is made up of more white matter connections, while the left hemisphere tends to have greater grey matter mass (Rourke & Conway, 1997). Accordingly, the right hemisphere will be more likely to be vulnerable to white matter disruption than the left hemisphere.

In the current study, white matter was associated with working memory and planning and the extent of grey matter abnormality was not significant after white matter abnormalities were statistically taken into account. Rourke and Conway's (1997) argument implies that disruptions in white matter development as a result of premature birth may have a greater impact on right as opposed to left hemisphere organisation, thereby leading to more specific impacts on visuo-spatial reasoning and the complex integration of information. Conceivably, more severe abnormalities will also be associated with injury to the left hemisphere, but this will be less profound in children with milder forms of early white matter disruption. In keeping with this hypothesis, forward Digit Span is generally affected only by more severe neurological disorder and both forward and backward span tend to be more affected by damage to the left hemisphere (Lezak et al., 2004). Therefore, hemispheric differences in white matter structure may help to explain why effect sizes for group differences on the Digit Span measure were smaller.

Apart from mathematics and reading, both executive attention and working memory/ planning abilities were shown to be associated with children's receptive language competence. The information that children were required to respond to on the standardised test of language comprehension consisted of complex sequences of instructions (e.g. point to the bird, then the girl wearing the hat and then the cat under the table) that would conceptually place heavy demands on both working memory and attention. One reason that this complex receptive language test was chosen is that it was felt that it would have a high degree of ecological validity. Children are likely to experience complex sequences of verbal instructions in the classroom environment. Findings suggest that the difficulties that children born very preterm experience in terms of organising complex information, sustaining attention and holding information in working memory are likely to lead to difficulties in the classroom setting. Coupled with strong associations with other areas of achievement, these findings support the third and final hypothesis that executive function would covary with children's academic achievement. Findings also support the independent utility of executive function measures in identifying children who are likely to be at risk of academic difficulties.

11.1.5 General Summary of Findings

Thus, many of the initial hypotheses for this research study were confirmed or partially supported. From the synopsis of findings reported above, we can start to envisage a conceptual model for findings, whereby predisposing factors such as maternal infection may confer a risk of neurological abnormality. However, the extent of children's immaturity and early exposure to the extra uterine environment also appear to be important in predicting later difficulties in attentional regulation. In some families, parent-child interactions may be intrusive, with low interactional synchrony. This means that children's independent problem solving and attentional regulation may be less scaffolded. As a result, key skills related to executive attention and working memory are lacking when these children enter formal schooling. Such findings have theoretical and applied implications that will be useful in our conceptualisation of and response to very preterm birth.

11.2.1 Theoretical Implications

The results from this study are consistent with current developmental theory. From a cognitive developmental standpoint, findings from this study are in line with the views of Case (1996), who argued that children's cognitive development is broadly dependent on the integration and coordination of several domain-specific conceptual structures. With neural maturation and experience, children become increasingly able to coordinate several pieces of information, which frees greater working memory capacity to devote to problem solving. This theory may be especially relevant for children's performance on the Tower of Hanoi task. With increasing demands on children's ability to coordinate several rules and obstacles, fewer children were able to complete the task. Case's principles suggest that differences in neural maturation, experience or both are likely to be constraining the working memory resources of children born very preterm, resulting in less efficient information processing and executive function.

This study also supports ecological (Bronfenbrenner & Morris, 1998) and dynamic systems models (Thelen & Smith, 1998), whereby children's growth and development is influenced by and exerts influence on several contextual factors. The mutual relationship between caregiver and child, in particular, was found to play an important role in the development of children's executive function, which in turn was associated with academic competence. As this is a correlational study, it cannot determine whether a more synchronous parent-child relationship assists neurological development and recovery or whether the difficulties that some of these children have as a result of white matter disruption make it difficult to read their signals and lead to poorer parent-child interactions. As suggested above, it is likely that the relationship is transactional, with the early interactive processes between child and primary caregiver helping to establish a platform for later cognitive development (Lyons-Ruth & Zeanah, 1993; Schore, 1994). Instability in the family system and parent-child systems was associated with poor outcome in the child, highlighting the view that children born very preterm operate within a matrix of contextual influences that are likely both to respond and contribute to differences in the trajectories of their development. From this study, it was also clear that children's difficulties were likely to be having an impact within the educational setting.

It is clear that neuropsychological theory, and specifically theories regarding the neurological and maturational underpinnings of executive function, can benefit from integration with developmental theory. Framing the ideas of neuropsychology within a contextual, systems model, illustrates how these ideas can complement and add to existing understandings of executive function and the mechanisms by which it might become compromised.

11.2.2 Applied Implications

Given that these theoretical models emphasise multiple, dynamic factors as contributing to development, it is also clear that there may be multiple points of entry for intervention with children born very preterm and their families. From a psychological perspective, this study suggests that one important target for intervention may be fostering parent-child synchrony during early childhood. As well as this, intervention efforts may also be focussed around supporting the development of executive skills in older children born very preterm. With regard to enhancing parent-child synchrony, it will be important to provide support to parents of children born very preterm during the course of neonatal intensive care to assist them to deal with grief, stress and anxiety associated with very preterm birth. Simultaneously, study findings stress the importance of ongoing practical advice and interactive training in order to assist parents to scaffold learning and effectively ‘read’ their children’s behavioural cues. To be most effective, intervention efforts should ideally be intense, multidisciplinary, well implemented and prolonged (Hess, 2005; Levy, Kim, & Olive, 2006; Olds, Sadler, & Kitzman, 2007). Findings from this study also indicated that parenting during toddlerhood and early childhood was related to later outcome, suggesting that this may be a sensitive period for intervention and surveillance.

In support of these comments, intervention studies have shown that changing parenting behaviours is effective in changing children’s behaviour (O'Connor, 2002; Olds et al., 2007). While past parenting-focussed intervention studies have failed to produce long term effects for children born preterm (McCarton, 1998; Olds et al., 2007), programs that are intense and individually focussed appear more promising. In a recent intervention study, mothers were taught to respond to their VLBW infants in a timely, reciprocal, supportive manner (Landry et al., 2006). At 3-month follow-up, children in the intervention group showed greater gains in cooperation, communication and positive affect across interactions with parents and testers, as well as greater levels of goal-directed focus in independent toy play compared to a placebo comparison group. Another NICU-based intervention program that focuses on teaching parents to monitor infants for signs of distress, has also been associated with better attentional and state regulation 2 years later. Importantly, infants who received this intervention showed corresponding neurological changes on EEG and structural MRI measures (Als et al., 2004; Als & Gilkerson, 1997; Assel et al., 2003). Although further research is needed, these studies suggest that parent-child interactive coaching may be effective in helping to optimise the cognitive and behavioural outcomes of children born very preterm.

Older children born very preterm may require guidance and training in executive function and self-regulatory skills. Studies have shown that teaching effective self-regulation skills can improve both academic performance and self-efficacy for students with learning difficulties (Montague, 2007; Schunk & Zimmerman, 2007; Zimmerman, 2002). Recent intervention techniques that have shown short-term effectiveness for the improvement of executive function include the ‘Tools of the Mind” curriculum (Bedrova & Leong, 2007) and computer based-training (Klingberg et al., 2005). “Tools of the Mind” is a preschool-based program that focuses on the use of external aids to promote attention, peer tutoring, modelling the use of private speech, dramatic play and games that involve inhibitory control and working memory skills. Using independent outcome measures that required inhibitory control and set shifting, Diamond, Barnett, Thomas, & Munro (2007) showed that this program was effective in enhancing the executive function performance of children who were engaged in the program relative to those who received the standard educational curriculum. Another recent study was conducted with older (7-12 year old) children with ADHD (Klingberg et al., 2005). The intervention condition involved 5 weeks of intensive practice on computer-based verbal and working memory tasks, which graduated in difficulty according to children's performance. Children who received the intervention showed improvement on several measures of executive function at immediate follow up and 3 months later.

Thus, whilst the current study suggests that there is scope for designing early intervention programs that address the relationship between parents and children, the finding of global executive working memory, planning and attention difficulties suggests that strategies that tackle these skills within traditional learning contexts may also be effective. Consequently, results of this study will be of benefit in informing theoretical and intervention models. Nonetheless, there are a number of limitations that should be considered in future research efforts and in the interpretation of study findings.

11.3 General Limitations

While some of the more specific limitations related to study findings have already been discussed, there are general limitations more common to the design and implementation of the research. These limitations predominantly relate to measurement, confounding factors, missing data and statistical analyses. Each of these issues will be discussed in turn.

11.3.1 Limitations in Instrumentation and Measurement

The first limitation of this study involves the paucity of reliable, standardised measures of executive function suitable for this age group. A strength of the measures incorporated in this study is that they are novel and based on neurodevelopmental theory. However, their psychometric properties are not well established. Given that there are no age-based reference norms or standards for any of the measures, it is difficult to determine how performance on one task may relate to performance on another. Similarly, while it is clear that children born very preterm group experienced difficulty in performing these tasks relative to their peers, it is difficult to ascertain the extent to which these differences represent developmental delay or atypical development. For example, children in both groups generally appeared to accomplish the various stages of the Detour Reaching Box with ease, with errors being uncommon. However, many children found the backward Digit Span task particularly difficult. This made comparison between performance on these tasks difficult. Because there is no reference standard for these measures, it is difficult to know whether better performance on the Detour Reaching Box task reflects a relative strength in the area of task switching and inhibitory control or whether this discrepancy reflects differences in the degree of difficulty of each task. Hence, while this study can certainly inform us as to between-group differences in executive function, it is restricted in terms of commenting on the clinical relevance of these difficulties or their relative interpretation in terms of the executive function profile of children born very preterm.

The large range of abilities in this particular sample may also have limited effective measurement and comparison of executive difficulties. Floor effects were evident for some of the measures, despite the fact that tests were selected from developmental literature based on a thorough investigation of the particular areas of executive function and academic achievement likely to be of importance in this age group. For example, several children were unable to understand instructions for the working memory tasks. Others appeared to show understanding, but then did not apply the instructions to the task. It is difficult to determine whether these difficulties are executive difficulties or whether they are the result of language processing impairments, difficulties in attention or other difficulties.

Limitations in reliability are also introduced when considering the composite measures of executive function derived from factor analysis in this study. This issue is compounded by the fact that the Detour Reaching Box was necessarily scored on an ordinal scale, while other measures, such as the K-CPT, produced continuous scores. In order to create comparable measures on a similar metric, the range and variance in scores for the K-CPT was necessarily restricted, which may have diminished the sensitivity of this measure for the detection of individual differences. In particular, the failure to find correlations between early neurological white and grey matter abnormalities on MRI and later executive attention may have been a function of the poorer reliability of this measure. Two measures were used to comprise the executive attention score, which may be insufficient to provide adequate representation of children’s ability to sustain and switch attention. Analyses indicated that the other factor, made up of four measures, was a more robust measure of executive performance. As this construct would have been more likely to detect individual differences, it is also likely that it would have been more sensitive to antecedent factors that were associated with these individual differences.

Further limitations of measurement relate to the construct validity of instruments. First, the underlying process of executive function is only accessible through behaviours elicited by the tasks. It is difficult to determine whether measures do indeed tap this construct. Executive function, by definition, relies on underlying processes, such as visual, motor and auditory information processing. These bottom-up processes, as opposed to executive coordination, may in fact be responsible for difficulties on the selected measures. Some support for a common, underlying construct for these processes was gleaned from a PCA and latent variable analysis of these measures. However, as has been recently suggested (van der Sluis et al., 2007), the correlations between measures of executive function may be the result of underlying correlations in other processes.

Added to this, executive function may be difficult to capture over the course of two hours. In many ways, individual differences in achievement are likely to come about through sustained motivation and effortful control. Fuster (2003), for example, has emphasised the role of executive function in controlling goal-directed behaviour over time. Individual differences in achievement may be as much explained by differences in stamina or delayed gratification over long delays. Whilst challenging to assess, these abilities should also ideally be taken into account in the conceptualisation of executive function. While we refer to tasks such as the K-CPT as measuring sustained attention, they certainly cannot capture the aspects of willpower, appreciation of long-term reward, sustained effort and motivation that undoubtedly characterise higher achievers. As Duncan (1986, p. 275) aptly comments, in a laboratory, the experimenter sets the goals whereas in real life people select their own goals and interests.

A further issue relates to the specificity of executive function measures for identifying children with academic difficulties. Although there were correlations between measures of executive function and academic achievement, suggesting some degree of sensitivity to individual differences, the specificity of these measures was not high. Neither working memory nor attention completely mediated the relationship between prematurity and mathematics. Furthermore, a large percentage of children who were classified as having low executive function abilities tended to fare well on measures of academic achievement. This lack of specificity will make it difficult to use these measures clinically in the identification of children who may have difficulties, suggesting that they currently be used alongside conventional measures to assist in the identification of specific problem-solving difficulties in children at risk of educational underachievement.

Finally, although previous literature on executive function and achievement indicates that early attention and executive skills are important precursors for academic development, these measures were administered contemporaneously in this study. Although it seems unlikely, the lack of effective control in this study design does not allow the ruling out of a reversed relationship, whereby academic knowledge may lead to better problem-solving abilities. In order to better identify causal relationships, further follow up and intervention research focussed on teaching children effective executive function skills and examining the effect on their academic performance will be important.

11.3.3 Limitations Associated with Confounding Factors

Together with limitations in measurement, the second set of limitations in this study relate to confounding factors and potential unidentified third variable influences. Premature birth can be seen as a risk factor for a range of different developmental outcomes. Children born very preterm are at risk for difficulties in visual processing. They are more likely to experience gross neurodevelopmental impairments, such as CP (Hack et al., 2000; Ross et al., 1991; van Baar et al., 2005; Wolke & Meyer, 1999), but this is likely to represent the more severe end of a spectrum of motor and visuo-spatial co-ordination difficulties (Foulder-Hughes & Cooke, 2003; Goyen et al., 1998; Hack et al., 1992; Sommerfelt, Markestad, & Ellersten, 1998). It is very difficult to separate difficulties with executive function from these broader outcomes. Difficulties with vision and motor control may have been relevant for some of these tests, despite the fact that steps were taken to prevent these factors from impacting on findings.

Added to this, several potentially influential factors were not considered in this study. In particular, no genetic information was collected. Research shows that certain allelic combinations increase vulnerability to low birth weight delivery in mothers who smoke during pregnancy (Wang, Zuckerman, Pearson, & Kaufman, 200). This is an important finding, in that it suggests that there may be a restriction of genetic variability associated with VLBW. Heritability studies have also indicated that genetic and environmental effects may have differential impacts, depending on the degree of prematurity (Koeppen-Schomerus, Eley, Wolke, Gringras, & Plomin, 2000). Thus, extreme medical or neurological compromise may restrict the ordinary genetic variability within this population. It is also possible that specific genes or gene-environment interactions moderate vulnerability to clinical risk and subsequent developmental impairments within children born very preterm. Therefore, genetic influences may help to account for heterogeneity in outcome in children born very preterm.

11.3.4 Limitations Associated with Missing Data

A third set of limitations of this study relate to missing data for antecedent experiences, as well as task measures. Follow-up rates are high for this cohort. However, results may be affected by the failure or inability of some children to complete tasks.

One child, for example, was necessarily excluded from analysis due to severe visual impairment. Other children were reluctant to complete tasks. This was particularly true for the CPT vigilance task, which many children in the very preterm group did not fully complete. Data loss is likely to have implications for the reliability of findings, especially when considering multivariate relationships between antecedent factors and executive outcomes. Of interest, children who refused to complete tasks were often those who showed low cognitive performance or who had performed poorly in past assessments. There is some evidence that lack of cooperation and engagement in early developmental assessments amongst children born very preterm may be associated with subsequent performance on cognitive tests (Wocaldo & Rieger, 2000). However, these authors caution that it is important to distinguish between task refusal and task failure in children.

In other cases, longitudinal data was unavailable. For example, while the inclusion of a control group enabled the comparison of groups across tasks, there was no MRI data for this group as they were recruited later in the study. While it is extremely uncommon, white matter pathology of the type seen in children born very preterm is also found among children born full term (Back, 2006). Having perinatal and neurological data available for the full term cohort would have allowed for the determination of whether the factors that were important in predicting outcomes in the preterm group were similar in the control group. This information would have increased power and allowed for the consideration of interactions between very preterm birth and socio-environmental risk factors.

11.3.6 Limitations in Statistical Analyses and Power

Finally, there were some limitations with regard to the statistical analyses and power in this study. Limitations of power may have been particularly influential in the analysis of predictors of executive function within the very preterm group. Often, small numbers of children experienced medical complications or interventions, thus reducing the likelihood that variations as a result of these medical complications would be detected by statistical tests. Similarly, the small numbers of children experiencing certain medical complications or adverse familial circumstances may have masked any interactional effects. One example of this was evident with regard to maternal depression. Children of mothers who had been chronically depressed through 2-6 years achieved much lower mean scores on the measure of executive working memory/ planning. However, only three mothers who had experienced this severe level of depression and the effect did not emerge as significant.

Added to this, limitations in the types of measures that executive function tasks afforded may have affected statistical tests through the violation of normal distribution assumptions. For instance, because the Detour Reaching Box Task was a progressive pass/fail task, scores could not be measured on an interval scale. In addition, most of the data from these tasks was not normally distributed. As would be expected, given the fact that this is a clinical population, children in the very preterm group often showed a greater variation in scores, while children in the full term control group often showed more skewed distributions. All findings were replicated using non-parametric tests, which supports the models presented. Nonetheless, these differences in distributions raise the possibility of specification errors, particularly for the later, multivariate analyses.

11.4. Research Implications and Directions for Future Study

Despite these limitations, the wealth and complexity of data make this a powerful longitudinal study. The research has broadened the understanding of relationships between early experiences associated with very preterm birth and later executive function. Findings also suggest several potential directions for future research. First, this research has established a risk of impairment in executive function as a broad construct. It may be useful for future studies to examine more specific dimensions of executive function in greater detail. For example, results suggested that children born very preterm were at greater risk of impairment in visuo-spatial working memory and sustained, focussed attention. More in-depth exploration and replication of these findings using a variety of measures of each of these specific domains would be a useful area for future consideration.

As well as this, future studies may benefit from the consideration of change and continuity of executive function over time. Only one study (Nosarti et al., 2007) has examined executive function in young adults born very preterm (<33 weeks GA). Despite a very high attrition rate in this sample, the study found clear discrepancies in the performance of children born very preterm on various measures of executive function, even after controlling IQ. Such findings suggest that the difficulties seen in the current, younger sample of children born very preterm are unlikely to be transient. However, the changing nature of executive function across the life course suggests that the nature and extent of impairments may vary age, with different factors affecting the development of these skills over time. As these children mature, it will be important to examine trajectories of skill development, as well as the family, social and schooling experiences that affect these trajectories.

Finally, longer term follow-up of study children will be important in determining the predictive utility of these early executive function measures for identifying children at risk of later academic difficulties. At this early stage of schooling, it is difficult for educationalists to discriminate between children whose difficulties are transient, and children who may require educational intervention in order to alter their developmental trajectories positively. Executive function is now widely recognised as being essential for successful transition to schooling in non-clinical samples, suggesting that executive difficulties at this early age will have long-term ramifications (Blair, 2002; Blair & Razza, 2007). Similarly, it would be useful to examine educational achievement in greater depth: micro longitudinal analyses of educational precursor skills, such as the development of mathematical strategies and concepts, may be of interest.

11.4 Conclusion

In a recent review, Masten and Obradovic (2006, p. 21) suggested that when learning (problem-solving and information processing), attachment, motivation, stress response, self-regulatory and family systems (along with school, peer and social systems) are intact, resilience in children is common. Unfortunately, this study and others have indicated that, for a large proportion of children born very preterm, many or all of these systems are compromised. The study demonstrated increased risk of impairment across a number of executive function domains and contexts in children born very preterm. Importantly, the impact of such difficulties was already apparent in the poor academic performance of many of these children. Findings suggest that the early detection of neurological abnormalities has prognostic value for identifying children most at risk. However, it is also clear that the family context, and particularly the quality of early parent-child relations, is also important in shaping the long term development of these high-risk children. While this thesis has focussed predominantly on the identification of difficulties in children born very preterm, there is a reference point for hope in the children who have managed to transition comfortably to school despite their compromised medical histories. As more and more children survive very preterm birth, the continued identification of factors that might buffer their vulnerabilities and ensure that they enjoy a chance of academic achievement and a sense of mastery will be paramount.

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Appendix A:

Glossary of Medical Terminology

Chorioamnionitis: An infection of the foetal membranes.

Chronic Lung Disease (CLD): Oxygen dependence at 36 weeks.

Continuous Positive Airways Pressure (CPAP): Gas is delivered to the lungs continuously with the aid of a nasal mask or endotracheal tube.

Intermittent Positive Pressure Ventilation (IPPV): The lungs are actively inflated during inhalation, with positive pressure ventilation delivered intermittently.

Intrauterine growth restriction (IUGR): Birthweight • 2SDs below expected birthweight for gestational age. Children who have IUGR are small for gestational age (SGA).

Intraventicular haemorrhage (IVH): Haemorrhage of the germinal matrix classified according to severity: Grade I - subependymal/germinal matrix haemorrhage, Grade II – Intraventricular bleeding without dilation, Grade III – Intraventricular bleeding with ventricular dilation, Grade IV – Intraventricular and parenchymal bleeding.

Necrotizing enterocolitis (NEC): An inflammatory condition of the small intestine and colon associated with immaturity.

Patent Ductus Arteriosis (PDA): A circulatory condition where the foetal blood vessel connecting the left pulmonary artery and aorta (the dutus arteriosis) does not close at birth.

Periventricular Leukomalasia (PVL): Injury of the periventricular white matter resulting in cysts at the corners of the lateral ventricles.

Respiratory Distress Syndrome (RDS): Condition in which the lungs are not sufficiently expanded due to a lack of surfactant.

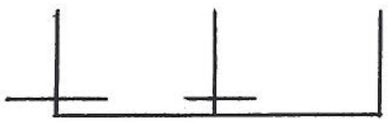
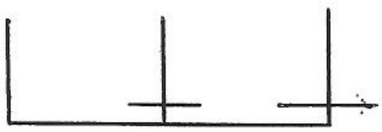
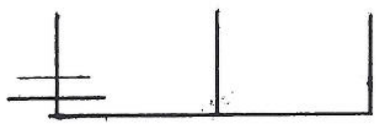
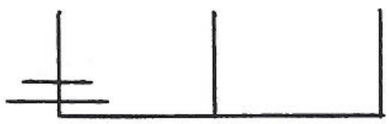
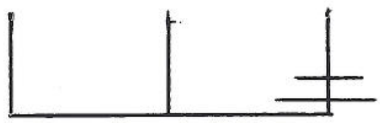
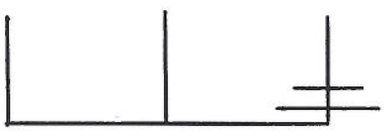
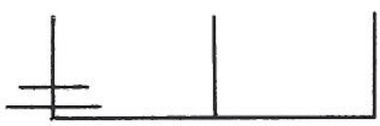
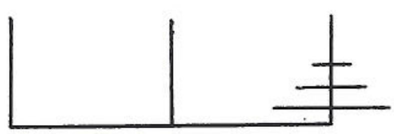
Retinopathy of prematurity (ROP): An eye disease that causes an alteration in the development of the retinal blood vessels.

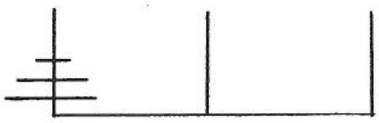
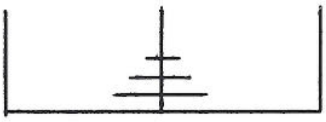
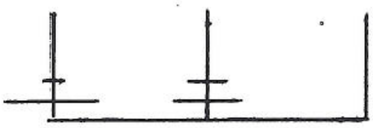
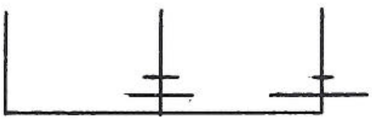
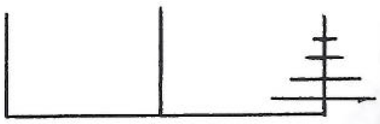
Sepsis: The presence of pathogenic micro-organisms or toxins in the blood.

Surfactant: Phospholipids in the alveoli and air passages that ensure elasticity.

Appendix B:

Start and End Goals for Trials of the Tower of Hanoi Task used to Assess Problem Solving in Children Born Very Preterm and Full Term at Age 6 Years

2-move level (Trial 1) Start 	Goal 
2-move level (Trial 2) Start 	Goal 
3-move level (Trial 1) Start 	Goal 
3-move level (Trial 2) Start 	Goal 
5-move level (Trial 1) Start 	Goal 

5-move level (Trial 2) Start 	Goal 
7-move level (Trial 1) Start 	Goal 
7-move level (Trial 2) Start 	Goal 
9-move level (Trial 1) Start 	Goal 
9-move level (Trial 2) Start 	Goal 
10-move level Start 	Goal 

Appendix C

Examiner Consensus Rating Scale for Executive Behaviour during Developmental Assessment of Children Born Very Preterm and Full Term at Age 6 Years

1) Initiation – Did the child ask for materials where appropriate and start the activities without significant cueing? Did they need to be coaxed to begin?

1 Consistently lacked initiative, needed several prompts and much encouragement
2 Seldom took initiative and needed some encouragement
3 Generally began tasks with much initiative, although this waned or fluctuated
4 Took initiative, asked for materials, needed no prompting

2) Inhibition – Was the child easily distracted by other things in the room? Did they sit back and think and activities, or start before instructions were finished? Did they grab at equipment or blurt out answers before thinking? Were they frequently out of their seats and did they frequently 'break rules' on executive function tasks?

1 Consistently showed low inhibitory control, was easily distracted and seemed 'blind' to behavioural consequences
2 Typically lacked forethought and became distracted by irrelevant stimuli at times
3 Generally showed appropriate inhibitory control
4 Consistently 'checked' behaviour before embarking on tasks

3) Sustained Attention – Did the child persist with tasks even when they reached greater levels of difficulty or were time-consuming? Did they begin converstations or questions that were not task-focussed?

1 Consistently inattentive, needed repeated prompting and coaxing to stay on task
2 Attended for short periods, but often became distracted or gave up when tasks became difficult
3 Generally attentive, with a few instances of off-task behaviour
4 Consistently attentive and on task

4) Self-monitoring – Was the child able to change their strategy when it became inappropriate? Were they aware of how they were doing on a task? Did they self-correct? Did they show high emotionality and frustration when tasks became difficult? Did they require a high level of supervision?

1 Unable to be left alone. Showed high emotionality and frustration and was difficult to calm.
2 Needed much supervision. Some instances when control was lacking
3 Was generally self-aware and able to regulate behaviour
4 Was adept at self-correcting, could state how they were doing on tasks showed optimal activity levels

5) Strategic behaviour/problem-solving – Did the child think flexibly about the problems or were they rigid and perseverative? Did they show problem-solving behaviours, such as self-talk, scratching head or counting on fingers?

1 Showed no evidence of planning or flexibility, perseverative and failed to try different options
2 Little evidence of problem sovling behaviour or deeper processing of instructions
3 Generally attempted to solve problems, but sometimes lacked flexibility or failed to plan
4 Consistently showed flexibility, strategised and changed behaviour when it failed to be productive

Appendix D

Revised Presentation Sheets for the Woodcock-Johnson III Maths Fluency Subtest

1 –1 =	0 + 3=	2 + 2=
4 -2 =	2 + 1=	3 - 3 =
0 + 0=	3 - 0 =	2 -1 =
2 + 4 =	5 + 0=	3 -1 =
1 + 6=	4 + 4 =	5 -0 =

1 + 1=	6 -1 =	3 + 5=
4 - 1 =	5 -2 =	3 -2 =
5 + 1=	6 -3 =	2 - 2 =
7 + 1=	4 -4 =	1 + 8=
4 -3 =	7 + 2=	4 + 1 =

2 + 5=	8 -1 =	5 -4 =
3 + 3=	10 -2 =	3+ 6 =
7 -2 =	2 + 8=	3 + 1=
9 -4 =	6 -2 =	4 + 6=
9 + 3=	8 -6 =	7 + 5=

Appendix E Correlations

Table E.1 Correlations between CompositeExecutive Function Scores and Clinical Factors within the Very Preterm Group

	Working memory/ planning factor	Executive attention factor	GA	BW	Male	Multi birth	IUGR	ANS	MC or fever	Infant sepsis	CLD	IPPV +CP AP	Surfa ct	PNS	NEC	PDA	ROP
Executive attention factor	.47																
Gestation	.12	.21															
Birthweight	.01	.12	.72														
Male gender	-.31	-.37	-.00	.09													
Multiple birth	.15	.02	.11	.09	-.06												
IUGR	-.01	-.18	-.02	-.37	.05	.04											
Antenatal steroids	.08	.16	-.05	-.03	-.22	.10	-.02										
Maternal chorioamniotis or fever	-.24	-.01	-.09	.11	-.07	-.16	-.14	.10									
Proven sepsis in infant	-.10	-.06	-.44	-.34	.06	-.14	-.02	-.06	.12								
CLD	.04	-.15	-.58	-.65	.08	-.11	.28	.04	-.05	.27							
Days on IPPV and CPAP	-.14	-.18	-.77	-.70	-.04	-.12	.14	-.01	.00	.41	.61						
RDS	-.05	-.19	-.35	-.34	-07	.03	-.02	-.18	.02	.17	.26	.44					
Postnatal steroids	-.06	-.08	-.40	-.30	.08	-.04	-.02	-.02	.14	.22	.42	.41	.23				
NEC	-.15	-.10	-.30	-.22	.03	.06	.03	.12	.23	.25	.13	.29	.09	.03			
PDA	-.01	-.19	-.48	-.35	-.07	-.01	-.06	.03	.04	.29	.26	.48	.38	.26	.25		
ROP	-.15	-.21	-.59	-.54	.09	-.10	.13	.05	.11	.33	.44	.59	.28	.40	.28	.27	
Smoking during preganancy	.10	-.08	.04	-.03	.07	.21	.18	.03	-.06	-.19	.03	-.02	.07	-.01	.03	-.06	-.05

Note. p<0.05. Spearman's rho correlations presented for dichotomous variables

Table E.2 Correlations between Composite Executive Function Scores and Neurological Factors (at Term Equivalent Age) within the Very Preterm Group

	Working memory/ planning factor	Executive attention factor	Brain vol.	WMA score	GMA score	IVH grade
Executive attention factor	.47					
Total brain volume	-.14	.10				
Total white matter abnormality score (MRI)	-29	-.10	-.04			
Total grey matter abnormality score (MRI)	-.17	-.19	-.04	.52		
Maximum grade IVH (Ultrasound)	-.32	-.06	.02	.53	.35	
PVL (Ultrasound)	-.26	-.12	.04	.44	.24	.25

Note. $p<0.05$. Spearman's rho correlations presented for dichotomous variables

Table E.3 Correlations between Composite Executive Function Scores and Socio-Familial Factors in the Very Preterm Group

	Working memory/ planning factor	Executive attention factor	SES (Early)	SES (Late)	Fam. finances	Mat educ.	Ethnic minor	Mat age <25	Single parent	P. change	Life stress	Mat. anxiey	Mat depress.	P. support	P intrude
Executive attention factor	.45														
SES (Early)	-.16	.04													
SES (6yrs)	-.15	.15	.82												
Family finances	-.05	.17	-.55	-.59											
Maternal education (2 yrs)	.09	-.12	-.55	-.55	-.43										
Ethnic minority	.07	-.18	-.03	-.07	-.08	-.04									
Maternal age <25 yrs	.01	-.09	-.17	-.16	.22	.20	.03								
Single parent (term)	.15	-.07	-.11	-.18	.44	.07	-.08	.12							
Parental change	-.28	.01	.29	.32	-.47	-.20	.12	-.26	-.45						
Life event stress	-.08	-.03	.10	.11	.11	.01	-.09	-.07	-.19	.30					
Ave. maternal anxiety score (1-6 yrs)	-.03	-.08	.20	.21	-38	-.06	.09	-.18	-.11	.33	.46				
Ave. maternal depression score (1-6 yrs)	-.07	-.02	.16	.17	-.12	-.06	.13	-.24	-.06	.24	.31	.61			
Parent supportive presence (2 & 4 yrs)	.22	.20	-.04	-.09	.10	.01	-.09	.11	-.05	-.05	-.15	-.10	-.14		
Parent intrusiveness (2 & 4 yrs)	-.33	-.25	.02	-.02	.00	.03	.21	-.31	.07	.02	.01	.06	.15	-.47	
Parent-child interactional synchrony	.33	.11	-.22	-.18	.18	.07	-.02	.02	.11	-.07	.05	-.13	-.20	.62	-.35

Note. p<0.05. Spearman's rho correlation coefficients presented for dichotomous variables

Table E4: Correlations between Executive Function, Academic Achievement and Child Neurodevelopmental Factors in Children born Very Preterm and Full Term

	Working memory/ plan	Exec. Attention	W.J Passage comp.	W.J Maths fluency	W.J. UDs.	Teacher rating - reading	Teacher rating – arithmetic.	Teacher rating - comp.	SES	IQ	CP	Visual lenses
Working memory/ planning composite		.42	.43	.53	.53	.33	.51	.30	-.05	.63	-	-.26
Executive attention composite	.47		.23	.34	.44	.13	.27	.12	-.03	.40	-	-.20
W.J. Passage comprehension	.56	.23		.53	.48	.72	.57	.45	-.15	.51	-	-.20
W.J. Maths fluency	.45	.26	.54		.49	.35	.62	.23	-.10	.56	-	-.21
W.J. Understanding directions	.55	.48	.40	.35		.34	.49	.31	-.17	.58	-	-.10
Teacher-rated reading	.64	.30	.74	.42	.49		.58	.65	.04	.49	-	-.13
Teacher-rated arithmetic	.59	.29	.57	.46	.42	.71		.53	.05	.57	-	-.28
Teacher-rated comprehension	.45	.33	.42	.27	.40	.64	.66		-.06	.45	-	-.17
Family SES	-.16	.04	-.17	-.03	-.28	-.27	-.25	-.13		-.09	-	-.15
IQ score	.60	.47	.48	.59	.55	.55	.52	.31	-.05		-	-.18
Severity of CP	-.34	-.09	-.27	-.22	-.26	-.31	-.30	-.11	.14	-.23		-
Visual impairment	-.22	.02	-.22	-.18	-.22	-.27	-.29	-.27	-.01	-.19	.15	

Note. Correlations within the group of children born very preterm are shown in black ink in bottom section of the table. Correlations within the group of children born full term are shown in blue in the top section of the table. W.J.: Woodcock-Johnson III. Spearman's Rho correlation coefficients presented for dichotomous variables.